

protein or with any fragment that contains the epitope. Preferably, the antigenic peptide comprises at least 10 amino acid residues, or at least 15 amino acid residues, or at least 20 amino acid residues, or at least 30 amino acid residues. Preferred epitopes encompassed by the antigenic peptide are regions of the protein that are located on its surface; commonly these are hydrophilic regions.

In certain embodiments of the invention, at least one epitope encompassed by the antigenic peptide is a region of NOVX-related protein that is located on the surface of the protein, *e.g.*, a hydrophilic region. A hydrophobicity analysis of the human NOVX-related protein sequence will indicate which regions of a NOVX-related protein are particularly hydrophilic and, therefore, are likely to encode surface residues useful for targeting antibody production. As a means for targeting antibody production, hydropathy plots showing regions of hydrophilicity and hydrophobicity may be generated by any method well known in the art, including, for example, the Kyte Doolittle or the Hopp Woods methods, either with or without Fourier transformation. See, *e.g.*, Hopp and Woods, 1981, *Proc. Nat. Acad. Sci. USA* 78: 3824-3828; Kyte and Doolittle 1982, *J. Mol. Biol.* 157: 105-142, each of which is incorporated herein by reference in its entirety. Antibodies that are specific for one or more domains within an antigenic protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

A protein of the invention, or a derivative, fragment, analog, homolog or ortholog thereof, may be utilized as an immunogen in the generation of antibodies that immunospecifically bind these protein components.

Various procedures known within the art may be used for the production of polyclonal or monoclonal antibodies directed against a protein of the invention, or against derivatives, fragments, analogs homologs or orthologs thereof (see, for example, *Antibodies: A Laboratory Manual*, Harlow and Lane, 1988, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, incorporated herein by reference). Some of these antibodies are discussed below.

Polyclonal Antibodies

For the production of polyclonal antibodies, various suitable host animals (*e.g.*, rabbit, goat, mouse or other mammal) may be immunized by one or more injections with the native protein, a synthetic variant thereof, or a derivative of the foregoing. An appropriate immunogenic preparation can contain, for example, the naturally occurring immunogenic protein, a chemically synthesized polypeptide representing the immunogenic protein, or a recombinantly expressed immunogenic protein. Furthermore, the protein may be conjugated

to a second protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. The preparation can further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (e.g., aluminum hydroxide), surface active substances (e.g., lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, etc.), adjuvants usable in humans such as Bacille Calmette-Guerin and *Corynebacterium parvum*, or similar immunostimulatory agents. Additional examples of adjuvants which can be employed include MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate).

The polyclonal antibody molecules directed against the immunogenic protein can be isolated from the mammal (e.g., from the blood) and further purified by well known techniques, such as affinity chromatography using protein A or protein G, which provide primarily the IgG fraction of immune serum. Subsequently, or alternatively, the specific antigen which is the target of the immunoglobulin sought, or an epitope thereof, may be immobilized on a column to purify the immune specific antibody by immunoaffinity chromatography. Purification of immunoglobulins is discussed, for example, by D. Wilkinson (*The Scientist*, published by The Scientist, Inc., Philadelphia PA, Vol. 14, No. 8 (April 17, 2000), pp. 25-28).

Monoclonal Antibodies

The term "monoclonal antibody" (MAb) or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one molecular species of antibody molecule consisting of a unique light chain gene product and a unique heavy chain gene product. In particular, the complementarity determining regions (CDRs) of the monoclonal antibody are identical in all the molecules of the population. MAbs thus contain an antigen binding site capable of immunoreacting with a particular epitope of the antigen characterized by a unique binding affinity for it.

Monoclonal antibodies can be prepared using hybridoma methods, such as those described by Kohler and Milstein, *Nature*, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes can be immunized in vitro.

The immunizing agent will typically include the protein antigen, a fragment thereof or a fusion protein thereof. Generally, either peripheral blood lymphocytes are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding, *MONOCLONAL ANTIBODIES: PRINCIPLES AND PRACTICE*, Academic Press, (1986) pp. 59-103). Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells can be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor, *J. Immunol.*, 133:3001 (1984); Brodeur et al., *MONOCLONAL ANTIBODY PRODUCTION TECHNIQUES AND APPLICATIONS*, Marcel Dekker, Inc., New York, (1987) pp. 51-63).

The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against the antigen. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, *Anal. Biochem.*, 107:220 (1980). Preferably, antibodies having a high degree of specificity and a high binding affinity for the target antigen are isolated.

After the desired hybridoma cells are identified, the clones can be subcloned by limiting dilution procedures and grown by standard methods. Suitable culture media for this

purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells can be grown in vivo as ascites in a mammal.

The monoclonal antibodies secreted by the subclones can be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies can also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA can be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also can be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences (U.S. Patent No. 4,816,567; Morrison, *Nature* 368, 812-13 (1994)) or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

Humanized Antibodies

The antibodies directed against the protein antigens of the invention can further comprise humanized antibodies or human antibodies. These antibodies are suitable for administration to humans without engendering an immune response by the human against the administered immunoglobulin. Humanized forms of antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')₂ or other antigen-binding subsequences of antibodies) that are principally comprised of the sequence of a human immunoglobulin, and contain minimal sequence derived from a non-human immunoglobulin. Humanization can be performed following the method of Winter and co-workers (Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-327 (1988); Verhoeyen et al., *Science*, 239:1534-1536 (1988)), by substituting rodent CDRs or CDR sequences for the

corresponding sequences of a human antibody. (See also U.S. Patent No. 5,225,539.) In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies can also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences.

5 In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the framework regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that

10 of a human immunoglobulin (Jones et al., 1986; Riechmann et al., 1988; and Presta, *Curr. Op. Struct. Biol.*, 2:593-596 (1992)).

Human Antibodies

Fully human antibodies relate to antibody molecules in which essentially the entire

15 sequences of both the light chain and the heavy chain, including the CDRs, arise from human genes. Such antibodies are termed "human antibodies", or "fully human antibodies" herein. Human monoclonal antibodies can be prepared by the trioma technique; the human B-cell hybridoma technique (see Kozbor, et al., 1983 *Immunol Today* 4: 72) and the EBV hybridoma technique to produce human monoclonal antibodies (see Cole, et al., 1985 In: MONOCLONAL

20 ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human monoclonal antibodies may be utilized in the practice of the present invention and may be produced by using human hybridomas (see Cote, et al., 1983. *Proc Natl Acad Sci USA* 80: 2026-2030) or by transforming human B-cells with Epstein Barr Virus in vitro (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96).

25 In addition, human antibodies can also be produced using additional techniques, including phage display libraries (Hoogenboom and Winter, *J. Mol. Biol.*, 227:381 (1991); Marks et al., *J. Mol. Biol.*, 222:581 (1991)). Similarly, human antibodies can be made by introducing human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon

30 challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in Marks et al. (*Bio/Technology* 10; 779-783 (1992)); Lonberg et al. (*Nature* 368 856-859 (1994)); Morrison (*Nature* 368, 812-13 (1994)); Fishwild

et al, (*Nature Biotechnology* 14, 845-51 (1996)); Neuberger (*Nature Biotechnology* 14, 826 (1996)); and Lonberg and Huszar (*Intern. Rev. Immunol.* 13 65-93 (1995)).

Human antibodies may additionally be produced using transgenic nonhuman animals which are modified so as to produce fully human antibodies rather than the animal's endogenous antibodies in response to challenge by an antigen. (See PCT publication WO94/02602). The endogenous genes encoding the heavy and light immunoglobulin chains in the nonhuman host have been incapacitated, and active loci encoding human heavy and light chain immunoglobulins are inserted into the host's genome. The human genes are incorporated, for example, using yeast artificial chromosomes containing the requisite human DNA segments. An animal which provides all the desired modifications is then obtained as progeny by crossbreeding intermediate transgenic animals containing fewer than the full complement of the modifications. The preferred embodiment of such a nonhuman animal is a mouse, and is termed the XenomouseTM as disclosed in PCT publications WO 96/33735 and WO 96/34096. This animal produces B cells which secrete fully human immunoglobulins. The antibodies can be obtained directly from the animal after immunization with an immunogen of interest, as, for example, a preparation of a polyclonal antibody, or alternatively from immortalized B cells derived from the animal, such as hybridomas producing monoclonal antibodies. Additionally, the genes encoding the immunoglobulins with human variable regions can be recovered and expressed to obtain the antibodies directly, or can be further modified to obtain analogs of antibodies such as, for example, single chain Fv molecules.

An example of a method of producing a nonhuman host, exemplified as a mouse, lacking expression of an endogenous immunoglobulin heavy chain is disclosed in U.S. Patent No. 5,939,598. It can be obtained by a method including deleting the J segment genes from at least one endogenous heavy chain locus in an embryonic stem cell to prevent rearrangement of the locus and to prevent formation of a transcript of a rearranged immunoglobulin heavy chain locus, the deletion being effected by a targeting vector containing a gene encoding a selectable marker; and producing from the embryonic stem cell a transgenic mouse whose somatic and germ cells contain the gene encoding the selectable marker.

A method for producing an antibody of interest, such as a human antibody, is disclosed in U.S. Patent No. 5,916,771. It includes introducing an expression vector that contains a nucleotide sequence encoding a heavy chain into one mammalian host cell in culture, introducing an expression vector containing a nucleotide sequence encoding a light chain into

another mammalian host cell, and fusing the two cells to form a hybrid cell. The hybrid cell expresses an antibody containing the heavy chain and the light chain.

In a further improvement on this procedure, a method for identifying a clinically relevant epitope on an immunogen, and a correlative method for selecting an antibody that binds immunospecifically to the relevant epitope with high affinity, are disclosed in PCT publication WO 99/53049.

F_{ab} Fragments and Single Chain Antibodies

According to the invention, techniques can be adapted for the production of single-chain antibodies specific to an antigenic protein of the invention (see e.g., U.S. Patent No. 4,946,778). In addition, methods can be adapted for the construction of F_{ab} expression libraries (see e.g., Huse, et al., 1989 Science 246: 1275-1281) to allow rapid and effective identification of monoclonal F_{ab} fragments with the desired specificity for a protein or derivatives, fragments, analogs or homologs thereof. Antibody fragments that contain the idiotype to a protein antigen may be produced by techniques known in the art including, but not limited to: (i) an F_{(ab')2} fragment produced by pepsin digestion of an antibody molecule; (ii) an F_{ab} fragment generated by reducing the disulfide bridges of an F_{(ab')2} fragment; (iii) an F_{ab} fragment generated by the treatment of the antibody molecule with papain and a reducing agent and (iv) F_v fragments.

Bispecific Antibodies

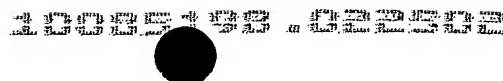
Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for an antigenic protein of the invention. The second binding target is any other antigen, and advantageously is a cell-surface protein or receptor or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities (Milstein and Cuello, *Nature*, 305:537-539 (1983)). Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker *et al.*, 1991 *EMBO J.*, 10:3655-3659.

According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (e.g. tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (e.g. alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. F(ab')₂ bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan et al., *Science* 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab')₂ fragments. These fragments are reduced in the presence of the dithiol com26S protease regulatory subunit 4g agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Additionally, Fab' fragments can be directly recovered from *E. coli* and chemically coupled to form bispecific antibodies. Shalaby et al., *J. Exp. Med.* 175:217-225 (1992) describe the production of a fully humanized bispecific antibody F(ab')₂ molecule. Each Fab'



fragment was separately secreted from *E. coli* and subjected to directed chemical coupling in vitro to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

5 Various techniques for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny et al., *J. Immunol.* 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. 10 This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger et al., *Proc. Natl. Acad. Sci. USA* 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) 15 by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber et al., *J. Immunol.* 152:5368 (1994).

20 Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt et al., *J. Immunol.* 147:60 (1991).

Exemplary bispecific antibodies can bind to two different epitopes, at least one of which originates in the protein antigen of the invention. Alternatively, an anti-antigenic arm of an immunoglobulin molecule can be combined with an arm which binds to a triggering 25 molecule on a leukocyte such as a T-cell receptor molecule (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular antigen. Bispecific antibodies can also be used to direct cytotoxic agents to cells which express a particular antigen. These antibodies possess an antigen-binding arm and an arm which binds a cytotoxic 30 agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the protein antigen described herein and further binds tissue factor (TF).

Heteroconjugate Antibodies

Heteroconjugate antibodies are also within the scope of the present invention.

Heteroconjugate antibodies are composed of two covalently joined antibodies. Such
 5 antibodies have, for example, been proposed to target immune system cells to unwanted cells
 (U.S. Patent No. 4,676,980), and for treatment of HIV infection (WO 91/00360; WO
 92/200373; EP 03089). It is contemplated that the antibodies can be prepared in vitro using
 known methods in synthetic protein chemistry, including those involving crosslinking agents.
 For example, immunotoxins can be constructed using a disulfide exchange reaction or by
 10 forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate
 and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No.
 4,676,980.

Effector Function Engineering

15 It can be desirable to modify the antibody of the invention with respect to effector
 function, so as to enhance, e.g., the effectiveness of the antibody in treating cancer. For
 example, cysteine residue(s) can be introduced into the Fc region, thereby allowing interchain
 disulfide bond formation in this region. The homodimeric antibody thus generated can have
 improved internalization capability and/or increased complement-mediated cell killing and
 20 antibody-dependent cellular cytotoxicity (ADCC). See Caron et al., J. Exp Med., 176: 1191-
 1195 (1992) and Shopes, J. Immunol., 148: 2918-2922 (1992). Homodimeric antibodies with
 enhanced anti-tumor activity can also be prepared using heterobifunctional cross-linkers as
 described in Wolff et al. Cancer Research, 53: 2560-2565 (1993). Alternatively, an antibody
 can be engineered that has dual Fc regions and can thereby have enhanced complement lysis
 25 and ADCC capabilities. See Stevenson et al., Anti-Cancer Drug Design, 3: 219-230 (1989).

Immunoconjugates

The invention also pertains to immunoconjugates comprising an antibody conjugated
 to a cytotoxic agent such as a chemotherapeutic agent, toxin (e.g., an enzymatically active
 30 toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive
 isotope (i.e., a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have
 been described above. Enzymatically active toxins and fragments thereof that can be used
 include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain

(from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, Aleurites fordii proteins, dianthin proteins, Phytolaca americana proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of
5 radionuclides are available for the production of radioconjugated antibodies. Examples include ^{212}Bi , ^{131}I , ^{131}In , ^{90}Y , and ^{186}Re .

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl
10 adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in
15 Vitetta et al., Science, 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

In another embodiment, the antibody can be conjugated to a "receptor" (such as streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is
20 administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (e.g., avidin) that is in turn conjugated to a cytotoxic agent.

In one embodiment, methods for the screening of antibodies that possess the desired specificity include, but are not limited to, enzyme-linked immunosorbent assay (ELISA) and
25 other immunologically-mediated techniques known within the art. In a specific embodiment, selection of antibodies that are specific to a particular domain of an NOVX protein is facilitated by generation of hybridomas that bind to the fragment of an NOVX protein possessing such a domain. Thus, antibodies that are specific for a desired domain within an NOVX protein, or derivatives, fragments, analogs or homologs thereof, are also provided
30 herein.

Anti-NOVX antibodies may be used in methods known within the art relating to the localization and/or quantitation of an NOVX protein (e.g., for use in measuring levels of the NOVX protein within appropriate physiological samples, for use in diagnostic methods, for use in imaging the protein, and the like). In a given embodiment, antibodies for NOVX

proteins, or derivatives, fragments, analogs or homologs thereof, that contain the antibody derived binding domain, are utilized as pharmacologically-active compounds (hereinafter "Therapeutics").

5 An anti-NOVX antibody (*e.g.*, monoclonal antibody) can be used to isolate an NOVX polypeptide by standard techniques, such as affinity chromatography or immunoprecipitation. An anti-NOVX antibody can facilitate the purification of natural NOVX polypeptide from cells and of recombinantly-produced NOVX polypeptide expressed in host cells. Moreover, an anti-NOVX antibody can be used to detect NOVX protein (*e.g.*, in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the NOVX
 10 protein. Anti-NOVX antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, *e.g.*, to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (*i.e.*, physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent
 15 materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, β -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example
 20 of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ^{125}I , ^{131}I , ^{35}S or ^3H .

NOVX Recombinant Expression Vectors and Host Cells

25 Another aspect of the invention pertains to vectors, preferably expression vectors, containing a nucleic acid encoding an NOVX protein, or derivatives, fragments, analogs or homologs thereof. As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA
 30 segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*, non-episomal mammalian vectors) are integrated into the genome of a host cell upon

introduction into the host cell, and thereby are replicated along with the host genome.

Moreover, certain vectors are capable of directing the expression of genes to which they are operatively-linked. Such vectors are referred to herein as "expression vectors". In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids.

5 In the present specification, "plasmid" and "vector" can be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors, such as viral vectors (*e.g.*, replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

10 The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, that is operatively-linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably-linked" is
15 sequence(s) in a manner that allows for expression of the nucleotide sequence (*e.g.*, in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell).

The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (*e.g.*, polyadenylation signals). Such regulatory sequences are
20 described, for example, in Goeddel, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990). Regulatory sequences include those that direct constitutive expression of a nucleotide sequence in many types of host cell and those that direct expression of the nucleotide sequence only in certain host cells (*e.g.*, tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the
25 design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc. The expression vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (*e.g.*, NOVX proteins, mutant forms of NOVX proteins, fusion proteins, etc.).

30 The recombinant expression vectors of the invention can be designed for expression of NOVX proteins in prokaryotic or eukaryotic cells. For example, NOVX proteins can be expressed in bacterial cells such as *Escherichia coli*, insect cells (using baculovirus expression vectors) yeast cells or mammalian cells. Suitable host cells are discussed further in Goeddel, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San

Diego, Calif. (1990). Alternatively, the recombinant expression vector can be transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

Expression of proteins in prokaryotes is most often carried out in *Escherichia coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: (i) to increase expression of recombinant protein; (ii) to increase the solubility of the recombinant protein; and (iii) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX (Pharmacia Biotech Inc; Smith and Johnson, 1988. *Gene* 67: 31-40), pMAL (New England Biolabs, Beverly, Mass.) and pRIT5 (Pharmacia, Piscataway, N.J.) that fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein.

Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc (Amrann *et al.*, (1988) *Gene* 69:301-315) and pET 11d (Studier *et al.*, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990) 60-89).

One strategy to maximize recombinant protein expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant protein. See, e.g., Gottesman, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990) 119-128. Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (see, e.g., Wada, *et al.*, 1992. *Nucl. Acids Res.* 20: 2111-2118). Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the NOVX expression vector is a yeast expression vector. Examples of vectors for expression in yeast *Saccharomyces cerevisiae* include pYepSec1 (Baldari, *et al.*, 1987. *EMBO J.* 6: 229-234), pMFa (Kurjan and Herskowitz, 1982. *Cell* 30: 933-943), pJRY88 (Schultz *et al.*, 1987. *Gene* 54: 113-123), pYES2 (Invitrogen Corporation, San Diego, Calif.), and picZ (InVitrogen Corp, San Diego, Calif.).



Alternatively, NOVX can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (*e.g.*, SF9 cells) include the pAc series (Smith, *et al.*, 1983. *Mol. Cell. Biol.* 3: 2156-2165) and the pVL series (Lucklow and Summers, 1989. *Virology* 170: 31-39).

5 In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed, 1987. *Nature* 329: 840) and pMT2PC (Kaufman, *et al.*, 1987. *EMBO J.* 6: 187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral regulatory elements. For example, commonly used promoters are
10 derived from polyoma, adenovirus 2, cytomegalovirus, and simian virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see, *e.g.*, Chapters 16 and 17 of Sambrook, *et al.*, MOLECULAR CLONING: A LABORATORY MANUAL. 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989.

In another embodiment, the recombinant mammalian expression vector is capable of
15 directing expression of the nucleic acid preferentially in a particular cell type (*e.g.*, tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert, *et al.*, 1987. *Genes Dev.* 1: 268-277), lymphoid-specific promoters (Calame and Eaton, 1988. *Adv. Immunol.* 43: 235-275), in particular promoters of T cell receptors (Winoto and Baltimore, 1989. *EMBO J.* 8: 729-733) and immunoglobulins (Banerji, *et al.*, 1983. *Cell* 33: 729-740; Queen and Baltimore, 1983. *Cell* 33: 741-748), neuron-specific promoters (*e.g.*, the neurofilament promoter; Byrne and Ruddle, 1989. *Proc. Natl. Acad. Sci. USA* 86: 5473-5477),
20 pancreas-specific promoters (Edlund, *et al.*, 1985. *Science* 230: 912-916), and mammary gland-specific promoters (*e.g.*, milk whey promoter; U.S. Pat. No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, *e.g.*, the murine hox promoters (Kessel and Gruss, 1990. *Science* 249: 374-379) and the α -fetoprotein promoter (Campes and Tilghman, 1989. *Genes Dev.* 3: 537-546).

The invention further provides a recombinant expression vector comprising a DNA
30 molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operatively-linked to a regulatory sequence in a manner that allows for expression (by transcription of the DNA molecule) of an RNA molecule that is antisense to NOVX mRNA. Regulatory sequences operatively linked to a nucleic acid cloned in the antisense orientation can be chosen that direct the continuous expression of the antisense RNA

molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen that direct constitutive, tissue specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes *see, e.g.,* Weintraub, *et al.*, "Antisense RNA as a molecular tool for genetic analysis," *Reviews-Trends in Genetics*, Vol. 1(1) 1986.

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but also to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic or eukaryotic cell. For example, NOVX protein can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (*e.g.,* DNA) into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, *et al.* (MOLECULAR CLONING: A LABORATORY MANUAL. 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate the foreign DNA into their genome. In order to identify and select these integrants, a gene that encodes a selectable marker (*e.g.,* resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Various selectable markers include those that confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid encoding a

selectable marker can be introduced into a host cell on the same vector as that encoding NOVX or can be introduced on a separate vector. Cells stably transfected with the introduced nucleic acid can be identified by drug selection (*e.g.*, cells that have incorporated the selectable marker gene will survive, while the other cells die).

5 A host cell of the invention, such as a prokaryotic or eukaryotic host cell in culture, can be used to produce (*i.e.*, express) NOVX protein. Accordingly, the invention further provides methods for producing NOVX protein using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of invention (into which a recombinant expression vector encoding NOVX protein has been introduced) in a suitable
10 medium such that NOVX protein is produced. In another embodiment, the method further comprises isolating NOVX protein from the medium or the host cell.

Transgenic NOVX Animals

The host cells of the invention can also be used to produce non-human transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or
15 an embryonic stem cell into which NOVX protein-coding sequences have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous NOVX sequences have been introduced into their genome or homologous recombinant animals in which endogenous NOVX sequences have been altered. Such animals are useful for studying the function and/or activity of NOVX protein and for identifying and/or
20 evaluating modulators of NOVX protein activity. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA that is integrated into the genome of a cell
25 from which a transgenic animal develops and that remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, a "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous NOVX gene has been altered by homologous recombination between the endogenous gene
30 and an exogenous DNA molecule introduced into a cell of the animal, *e.g.*, an embryonic cell of the animal, prior to development of the animal.

A transgenic animal of the invention can be created by introducing NOVX-encoding nucleic acid into the male pronuclei of a fertilized oocyte (*e.g.*, by microinjection, retroviral

infection) and allowing the oocyte to develop in a pseudopregnant female foster animal. The human NOVX cDNA sequences SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, and 31 can be introduced as a transgene into the genome of a non-human animal.

Alternatively, a non-human homologue of the human NOVX gene, such as a mouse NOVX gene, can be isolated based on hybridization to the human NOVX cDNA (described further *supra*) and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably-linked to the NOVX transgene to direct expression of NOVX protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866; 4,870,009; and 4,873,191; and Hogan, 1986. In: MANIPULATING THE MOUSE EMBRYO, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the NOVX transgene in its genome and/or expression of NOVX mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene-encoding NOVX protein can further be bred to other transgenic animals carrying other transgenes.

To create a homologous recombinant animal, a vector is prepared which contains at least a portion of an NOVX gene into which a deletion, addition or substitution has been introduced to thereby alter, *e.g.*, functionally disrupt, the NOVX gene. The NOVX gene can be a human gene (*e.g.*, the cDNA of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, and 31), but more preferably, is a non-human homologue of a human NOVX gene. For example, a mouse homologue of human NOVX gene of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, and 31 can be used to construct a homologous recombination vector suitable for altering an endogenous NOVX gene in the mouse genome. In one embodiment, the vector is designed such that, upon homologous recombination, the endogenous NOVX gene is functionally disrupted (*i.e.*, no longer encodes a functional protein; also referred to as a "knock out" vector).

Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous NOVX gene is mutated or otherwise altered but still encodes functional protein (*e.g.*, the upstream regulatory region can be altered to thereby alter the expression of the endogenous NOVX protein). In the homologous recombination vector, the altered portion

of the NOVX gene is flanked at its 5'- and 3'-termini by additional nucleic acid of the NOVX gene to allow for homologous recombination to occur between the exogenous NOVX gene carried by the vector and an endogenous NOVX gene in an embryonic stem cell. The additional flanking NOVX nucleic acid is of sufficient length for successful homologous recombination with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5'- and 3'-termini) are included in the vector. *See, e.g., Thomas, et al., 1987. Cell 51: 503* for a description of homologous recombination vectors. The vector is then introduced into an embryonic stem cell line (*e.g., by electroporation*) and cells in which the introduced NOVX gene has homologously-recombined with the endogenous NOVX gene are selected. *See, e.g., Li, et al., 1992. Cell 69: 915.*

The selected cells are then injected into a blastocyst of an animal (*e.g., a mouse*) to form aggregation chimeras. *See, e.g., Bradley, 1987. In: TERATOCARCINOMAS AND EMBRYONIC STEM CELLS: A PRACTICAL APPROACH, Robertson, ed. IRL, Oxford, pp. 113-152.* A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term. Progeny harboring the homologously-recombined DNA in their germ cells can be used to breed animals in which all cells of the animal contain the homologously-recombined DNA by germline transmission of the transgene. Methods for constructing homologous recombination vectors and homologous recombinant animals are described further in Bradley, 1991. *Curr. Opin. Biotechnol. 2: 823-829*; PCT International Publication Nos.: WO 90/11354; WO 91/01140; WO 92/0968; and WO 93/04169.

In another embodiment, transgenic non-humans animals can be produced that contain selected systems that allow for regulated expression of the transgene. One example of such a system is the cre/loxP recombinase system of bacteriophage P1. For a description of the cre/loxP recombinase system, *See, e.g., Lakso, et al., 1992. Proc. Natl. Acad. Sci. USA 89: 6232-6236.* Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae*. *See, O'Gorman, et al., 1991. Science 251:1351-1355.* If a cre/loxP recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, *e.g., by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.*

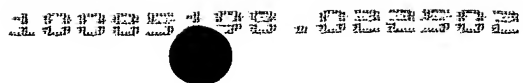
Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut, *et al., 1997. Nature 385: 810-813.* In brief, a cell (*e.g., a somatic cell*) from the transgenic animal can be isolated and induced to exit the

growth cycle and enter G₀ phase. The quiescent cell can then be fused, *e.g.*, through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyte and then transferred to pseudopregnant female foster animal. The
 5 offspring borne of this female foster animal will be a clone of the animal from which the cell (*e.g.*, the somatic cell) is isolated.

Pharmaceutical Compositions

The NOVX nucleic acid molecules, NOVX proteins, and anti-NOVX antibodies (also referred to herein as "active compounds") of the invention, and derivatives, fragments, analogs
 10 and homologs thereof, can be incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier. As used herein, "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like,
 15 compatible with pharmaceutical administration. Suitable carriers are described in the most recent edition of Remington's Pharmaceutical Sciences, a standard reference text in the field, which is incorporated herein by reference. Preferred examples of such carriers or diluents include, but are not limited to, water, saline, finger's solutions, dextrose solution, and 5% human serum albumin. Liposomes and non-aqueous vehicles such as fixed oils may also be
 20 used. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

A pharmaceutical composition of the invention is formulated to be compatible with its
 25 intended route of administration. Examples of routes of administration include parenteral, *e.g.*, intravenous, intradermal, subcutaneous, oral (*e.g.*, inhalation), transdermal (*i.e.*, topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine,
 30 propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid (EDTA); buffers such as acetates, citrates or phosphates, and agents for the adjustment of tonicity such as sodium chloride or dextrose. The pH can be

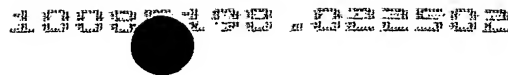


adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, N.J.) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringeability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as manitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (*e.g.*, an NOVX protein or anti-NOVX antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, methods of preparation are vacuum drying and freeze-drying that yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form



of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

For administration by inhalation, the compounds are delivered in the form of an aerosol spray from pressured container or dispenser which contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

The compounds can also be prepared in the form of suppositories (*e.g.*, with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

The nucleic acid molecules of the invention can be inserted into vectors and used as gene therapy vectors. Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (*see, e.g.*, U.S. Patent No. 5,328,470) or by stereotactic injection (*see, e.g.*, Chen, *et al.*, 1994. *Proc. Natl. Acad. Sci. USA* 91: 3054-3057). The pharmaceutical preparation of the gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant cells, *e.g.*, retroviral vectors, the pharmaceutical preparation can include one or more cells that produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

Screening and Detection Methods

The isolated nucleic acid molecules of the invention can be used to express NOVX protein (*e.g.*, via a recombinant expression vector in a host cell in gene therapy applications), to detect NOVX mRNA (*e.g.*, in a biological sample) or a genetic lesion in an NOVX gene, and to modulate NOVX activity, as described further, below. In addition, the NOVX proteins can be used to screen drugs or compounds that modulate the NOVX protein activity or expression as well as to treat disorders characterized by insufficient or excessive production of NOVX protein or production of NOVX protein forms that have decreased or aberrant activity compared to NOVX wild-type protein (*e.g.*; diabetes (regulates insulin release); obesity (binds and transport lipids); metabolic disturbances associated with obesity, the metabolic syndrome X as well as anorexia and wasting disorders associated with chronic diseases and various cancers, and infectious disease (possesses anti-microbial activity) and the various dyslipidemias. In addition, the anti-NOVX antibodies of the invention can be used to detect

and isolate NOVX proteins and modulate NOVX activity. In yet a further aspect, the invention can be used in methods to influence appetite, absorption of nutrients and the disposition of metabolic substrates in both a positive and negative fashion.

5 The invention further pertains to novel agents identified by the screening assays described herein and uses thereof for treatments as described, *supra*.

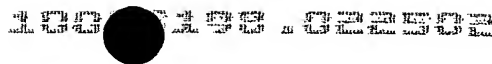
Screening Assays

10 The invention provides a method (also referred to herein as a "screening assay") for identifying modulators, *i.e.*, candidate or test compounds or agents (*e.g.*, peptides, peptidomimetics, small molecules or other drugs) that bind to NOVX proteins or have a stimulatory or inhibitory effect on, *e.g.*, NOVX protein expression or NOVX protein activity. The invention also includes compounds identified in the screening assays described herein.

15 In one embodiment, the invention provides assays for screening candidate or test compounds which bind to or modulate the activity of the membrane-bound form of an NOVX protein or polypeptide or biologically-active portion thereof. The test compounds of the invention can be obtained using any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; the "one-bead one-compound" library method; and synthetic library methods using affinity
20 chromatography selection. The biological library approach is limited to peptide libraries, while the other four approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds. *See, e.g.*, Lam, 1997. *Anticancer Drug Design* 12: 145.

A "small molecule" as used herein, is meant to refer to a composition that has a molecular weight of less than about 5 kD and most preferably less than about 4 kD. Small
25 molecules can be, *e.g.*, nucleic acids, peptides, polypeptides, peptidomimetics, carbohydrates, lipids or other organic or inorganic molecules. Libraries of chemical and/or biological mixtures, such as fungal, bacterial, or algal extracts, are known in the art and can be screened with any of the assays of the invention.

30 Examples of methods for the synthesis of molecular libraries can be found in the art, for example in: DeWitt, *et al.*, 1993. *Proc. Natl. Acad. Sci. U.S.A.* 90: 6909; Erb, *et al.*, 1994. *Proc. Natl. Acad. Sci. U.S.A.* 91: 11422; Zuckermann, *et al.*, 1994. *J. Med. Chem.* 37: 2678; Cho, *et al.*, 1993. *Science* 261: 1303; Carrell, *et al.*, 1994. *Angew. Chem. Int. Ed. Engl.* 33: 2059; Carell, *et al.*, 1994. *Angew. Chem. Int. Ed. Engl.* 33: 2061; and Gallop, *et al.*, 1994. *J. Med. Chem.* 37: 1233.



Libraries of compounds may be presented in solution (e.g., Houghten, 1992. *Biotechniques* 13: 412-421), or on beads (Lam, 1991. *Nature* 354: 82-84), on chips (Fodor, 1993. *Nature* 364: 555-556), bacteria (Ladner, U.S. Patent No. 5,223,409), spores (Ladner, U.S. Patent 5,233,409), plasmids (Cull, *et al.*, 1992. *Proc. Natl. Acad. Sci. USA* 89: 1865-1869) or on phage (Scott and Smith, 1990. *Science* 249: 386-390; Devlin, 1990. *Science* 249: 404-406; Cwirla, *et al.*, 1990. *Proc. Natl. Acad. Sci. U.S.A.* 87: 6378-6382; Felici, 1991. *J. Mol. Biol.* 222: 301-310; Ladner, U.S. Patent No. 5,233,409.).

In one embodiment, an assay is a cell-based assay in which a cell which expresses a membrane-bound form of NOVX protein, or a biologically-active portion thereof, on the cell surface is contacted with a test compound and the ability of the test compound to bind to an NOVX protein determined. The cell, for example, can be of mammalian origin or a yeast cell. Determining the ability of the test compound to bind to the NOVX protein can be accomplished, for example, by coupling the test compound with a radioisotope or enzymatic label such that binding of the test compound to the NOVX protein or biologically-active portion thereof can be determined by detecting the labeled compound in a complex. For example, test compounds can be labeled with ^{125}I , ^{35}S , ^{14}C , or ^3H , either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, test compounds can be enzymatically-labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product. In one embodiment, the assay comprises contacting a cell which expresses a membrane-bound form of NOVX protein, or a biologically-active portion thereof, on the cell surface with a known compound which binds NOVX to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an NOVX protein, wherein determining the ability of the test compound to interact with an NOVX protein comprises determining the ability of the test compound to preferentially bind to NOVX protein or a biologically-active portion thereof as compared to the known compound.

In another embodiment, an assay is a cell-based assay comprising contacting a cell expressing a membrane-bound form of NOVX protein, or a biologically-active portion thereof, on the cell surface with a test compound and determining the ability of the test compound to modulate (e.g., stimulate or inhibit) the activity of the NOVX protein or biologically-active portion thereof. Determining the ability of the test compound to modulate the activity of NOVX or a biologically-active portion thereof can be accomplished, for example, by determining the ability of the NOVX protein to bind to or interact with an NOVX target

molecule. As used herein, a "target molecule" is a molecule with which an NOVX protein binds or interacts in nature, for example, a molecule on the surface of a cell which expresses an NOVX interacting protein, a molecule on the surface of a second cell, a molecule in the extracellular milieu, a molecule associated with the internal surface of a cell membrane or a cytoplasmic molecule. An NOVX target molecule can be a non-NOVX molecule or an NOVX protein or polypeptide of the invention. In one embodiment, an NOVX target molecule is a component of a signal transduction pathway that facilitates transduction of an extracellular signal (*e.g.* a signal generated by binding of a compound to a membrane-bound NOVX molecule) through the cell membrane and into the cell. The target, for example, can be a second intercellular protein that has catalytic activity or a protein that facilitates the association of downstream signaling molecules with NOVX.

Determining the ability of the NOVX protein to bind to or interact with an NOVX target molecule can be accomplished by one of the methods described above for determining direct binding. In one embodiment, determining the ability of the NOVX protein to bind to or interact with an NOVX target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the target (*i.e.* intracellular Ca^{2+} , diacylglycerol, IP_3 , etc.), detecting catalytic/enzymatic activity of the target an appropriate substrate, detecting the induction of a reporter gene (comprising an NOVX-responsive regulatory element operatively linked to a nucleic acid encoding a detectable marker, *e.g.*, luciferase), or detecting a cellular response, for example, cell survival, cellular differentiation, or cell proliferation.

In yet another embodiment, an assay of the invention is a cell-free assay comprising contacting an NOVX protein or biologically-active portion thereof with a test compound and determining the ability of the test compound to bind to the NOVX protein or biologically-active portion thereof. Binding of the test compound to the NOVX protein can be determined either directly or indirectly as described above. In one such embodiment, the assay comprises contacting the NOVX protein or biologically-active portion thereof with a known compound which binds NOVX to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an NOVX protein, wherein determining the ability of the test compound to interact with an NOVX protein comprises determining the ability of the test compound to preferentially bind to NOVX or biologically-active portion thereof as compared to the known compound.

In still another embodiment, an assay is a cell-free assay comprising contacting NOVX protein or biologically-active portion thereof with a test compound and determining the ability of the test compound to modulate (*e.g.* stimulate or inhibit) the activity of the NOVX protein or biologically-active portion thereof. Determining the ability of the test compound to modulate the activity of NOVX can be accomplished, for example, by determining the ability of the NOVX protein to bind to an NOVX target molecule by one of the methods described above for determining direct binding. In an alternative embodiment, determining the ability of the test compound to modulate the activity of NOVX protein can be accomplished by determining the ability of the NOVX protein further modulate an NOVX target molecule. For example, the catalytic/enzymatic activity of the target molecule on an appropriate substrate can be determined as described, *supra*.

In yet another embodiment, the cell-free assay comprises contacting the NOVX protein or biologically-active portion thereof with a known compound which binds NOVX protein to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an NOVX protein, wherein determining the ability of the test compound to interact with an NOVX protein comprises determining the ability of the NOVX protein to preferentially bind to or modulate the activity of an NOVX target molecule.

The cell-free assays of the invention are amenable to use of both the soluble form or the membrane-bound form of NOVX protein. In the case of cell-free assays comprising the membrane-bound form of NOVX protein, it may be desirable to utilize a solubilizing agent such that the membrane-bound form of NOVX protein is maintained in solution. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide, Triton[®] X-100, Triton[®] X-114, Thesit[®], Isotridecypoly(ethylene glycol ether)_n, N-dodecyl--N,N-dimethyl-3-ammonio-1-propane sulfonate, 3-(3-cholamidopropyl) dimethylamminiol-1-propane sulfonate (CHAPS), or 3-(3-cholamidopropyl)dimethylamminiol-2-hydroxy-1-propane sulfonate (CHAPSO).

In more than one embodiment of the above assay methods of the invention, it may be desirable to immobilize either NOVX protein or its target molecule to facilitate separation of complexed from uncomplexed forms of one or both of the proteins, as well as to accommodate automation of the assay. Binding of a test compound to NOVX protein, or interaction of NOVX protein with a target molecule in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for containing the reactants. Examples of such

vessels include microtiter plates, test tubes, and micro-centrifuge tubes. In one embodiment, a fusion protein can be provided that adds a domain that allows one or both of the proteins to be bound to a matrix. For example, GST-NOVX fusion proteins or GST-target fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or
5 glutathione derivatized microtiter plates, that are then combined with the test compound or the test compound and either the non-adsorbed target protein or NOVX protein, and the mixture is incubated under conditions conducive to complex formation (*e.g.*, at physiological conditions for salt and pH). Following incubation, the beads or microtiter plate wells are washed to remove any unbound components, the matrix immobilized in the case of beads, complex
10 determined either directly or indirectly, for example, as described, *supra*. Alternatively, the complexes can be dissociated from the matrix, and the level of NOVX protein binding or activity determined using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either the NOVX protein or its target
15 molecule can be immobilized utilizing conjugation of biotin and streptavidin. Biotinylated NOVX protein or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques well-known within the art (*e.g.*, biotinylation kit, Pierce Chemicals, Rockford, Ill.), and immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical). Alternatively, antibodies reactive with NOVX protein or target
20 molecules, but which do not interfere with binding of the NOVX protein to its target molecule, can be derivatized to the wells of the plate, and unbound target or NOVX protein trapped in the wells by antibody conjugation. Methods for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the NOVX protein or target molecule, as well as enzyme-linked
25 assays that rely on detecting an enzymatic activity associated with the NOVX protein or target molecule.

In another embodiment, modulators of NOVX protein expression are identified in a method wherein a cell is contacted with a candidate compound and the expression of NOVX mRNA or protein in the cell is determined. The level of expression of NOVX mRNA or
30 protein in the presence of the candidate compound is compared to the level of expression of NOVX mRNA or protein in the absence of the candidate compound. The candidate compound can then be identified as a modulator of NOVX mRNA or protein expression based upon this comparison. For example, when expression of NOVX mRNA or protein is greater (*i.e.*, statistically significantly greater) in the presence of the candidate compound than in its

absence, the candidate compound is identified as a stimulator of NOVX mRNA or protein expression. Alternatively, when expression of NOVX mRNA or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate compound is identified as an inhibitor of NOVX mRNA or protein expression. The level of NOVX mRNA or protein expression in the cells can be determined by methods described herein for detecting NOVX mRNA or protein.

In yet another aspect of the invention, the NOVX proteins can be used as "bait proteins" in a two-hybrid assay or three hybrid assay (*see, e.g.*, U.S. Patent No. 5,283,317; Zervos, *et al.*, 1993. *Cell* 72: 223-232; Madura, *et al.*, 1993. *J. Biol. Chem.* 268: 12046-12054; Bartel, *et al.*, 1993. *Biotechniques* 14: 920-924; Iwabuchi, *et al.*, 1993. *Oncogene* 8: 1693-1696; and Brent WO 94/10300), to identify other proteins that bind to or interact with NOVX ("NOVX-binding proteins" or "NOVX-bp") and modulate NOVX activity. Such NOVX-binding proteins are also likely to be involved in the propagation of signals by the NOVX proteins as, for example, upstream or downstream elements of the NOVX pathway.

The two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for NOVX is fused to a gene encoding the DNA binding domain of a known transcription factor (*e.g.*, GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If the "bait" and the "prey" proteins are able to interact, *in vivo*, forming an NOVX-dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (*e.g.*, LacZ) that is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene that encodes the protein which interacts with NOVX.

The invention further pertains to novel agents identified by the aforementioned screening assays and uses thereof for treatments as described herein.

Detection Assays

Portions or fragments of the cDNA sequences identified herein (and the corresponding complete gene sequences) can be used in numerous ways as polynucleotide reagents. By way of example, and not of limitation, these sequences can be used to: (i) map their respective

genes on a chromosome; and, thus, locate gene regions associated with genetic disease; (ii) identify an individual from a minute biological sample (tissue typing); and (iii) aid in forensic identification of a biological sample. Some of these applications are described in the subsections, below.

5

Chromosome Mapping

Once the sequence (or a portion of the sequence) of a gene has been isolated, this sequence can be used to map the location of the gene on a chromosome. This process is called chromosome mapping. Accordingly, portions or fragments of the NOVX sequences, SEQ ID
10 NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, and 31, or fragments or derivatives thereof, can be used to map the location of the NOVX genes, respectively, on a chromosome. The mapping of the NOVX sequences to chromosomes is an important first step in correlating these sequences with genes associated with disease.

Briefly, NOVX genes can be mapped to chromosomes by preparing PCR primers
15 (preferably 15-25 bp in length) from the NOVX sequences. Computer analysis of the NOVX, sequences can be used to rapidly select primers that do not span more than one exon in the genomic DNA, thus complicating the amplification process. These primers can then be used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the NOVX sequences will yield an
20 amplified fragment.

Somatic cell hybrids are prepared by fusing somatic cells from different mammals (e.g., human and mouse cells). As hybrids of human and mouse cells grow and divide, they gradually lose human chromosomes in random order, but retain the mouse chromosomes. By using media in which mouse cells cannot grow, because they lack a particular enzyme, but in
25 which human cells can, the one human chromosome that contains the gene encoding the needed enzyme will be retained. By using various media, panels of hybrid cell lines can be established. Each cell line in a panel contains either a single human chromosome or a small number of human chromosomes, and a full set of mouse chromosomes, allowing easy mapping of individual genes to specific human chromosomes. See, e.g., D'Eustachio, *et al.*,
30 1983. *Science* 220: 919-924. Somatic cell hybrids containing only fragments of human chromosomes can also be produced by using human chromosomes with translocations and deletions.

PCR mapping of somatic cell hybrids is a rapid procedure for assigning a particular sequence to a particular chromosome. Three or more sequences can be assigned per day using

Fluorescence *in situ* hybridization (FISH) of a DNA sequence to a metaphase chromosomal spread can further be used to provide a precise chromosomal location in one step. Chromosome spreads can be made using cells whose division has been blocked in metaphase by a chemical like colcemid that disrupts the mitotic spindle. The chromosomes can be treated briefly with trypsin, and then stained with Giemsa. A pattern of light and dark bands develops on each chromosome, so that the chromosomes can be identified individually. The FISH technique can be used with a DNA sequence as short as 500 or 600 bases.

Reagents for chromosome mapping can be used individually to mark a single chromosome or a single site on that chromosome, or panels of reagents can be used for marking multiple sites and/or multiple chromosomes. Reagents corresponding to noncoding regions of the genes actually are preferred for mapping purposes. Coding sequences are more likely to be conserved within gene families, thus increasing the chance of cross hybridizations during chromosomal mapping.

Moreover, differences in the DNA sequences between individuals affected and unaffected with a disease associated with the NOVX gene, can be determined. If a mutation is observed in some or all of the affected individuals but not in any unaffected individuals, then the mutation is likely to be the causative agent of the particular disease. Comparison of affected and unaffected individuals generally involves first looking for structural alterations in the chromosomes, such as deletions or translocations that are visible from chromosome spreads or detectable using PCR based on that DNA sequence. Ultimately, complete

sequencing of genes from several individuals can be performed to confirm the presence of a mutation and to distinguish mutations from polymorphisms.

Tissue Typing

5 The NOVX sequences of the invention can also be used to identify individuals from minute biological samples. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification. The sequences of the invention are useful as additional DNA markers for RFLP ("restriction fragment length polymorphisms," described in U.S. Patent No. 5,272,057).

10 Furthermore, the sequences of the invention can be used to provide an alternative technique that determines the actual base-by-base DNA sequence of selected portions of an individual's genome. Thus, the NOVX sequences described herein can be used to prepare two PCR primers from the 5'- and 3'-termini of the sequences. These primers can then be used to amplify an individual's DNA and subsequently sequence it.

15 Panels of corresponding DNA sequences from individuals, prepared in this manner, can provide unique individual identifications, as each individual will have a unique set of such DNA sequences due to allelic differences. The sequences of the invention can be used to obtain such identification sequences from individuals and from tissue. The NOVX sequences of the invention uniquely represent portions of the human genome. Allelic variation occurs to some degree in the coding regions of these sequences, and to a greater degree in the noncoding regions. It is estimated that allelic variation between individual humans occurs with a frequency of about once per each 500 bases. Much of the allelic variation is due to single nucleotide polymorphisms (SNPs), which include restriction fragment length polymorphisms (RFLPs).

20 Each of the sequences described herein can, to some degree, be used as a standard against which DNA from an individual can be compared for identification purposes. Because greater numbers of polymorphisms occur in the noncoding regions, fewer sequences are necessary to differentiate individuals. The noncoding sequences can comfortably provide positive individual identification with a panel of perhaps 10 to 1,000 primers that each yield a noncoding amplified sequence of 100 bases. If predicted coding sequences, such as those in SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, and 31 are used, a more appropriate number of primers for positive individual identification would be 500-2,000.

Predictive Medicine

The invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical trials are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the invention relates to diagnostic assays for determining NOVX protein and/or nucleic acid expression as well as NOVX activity, in the context of a biological sample (*e.g.*, blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant NOVX expression or activity. The disorders include metabolic disorders, diabetes, obesity, infectious disease, anorexia, cancer-associated cachexia, cancer, neurodegenerative disorders, Alzheimer's Disease, Parkinson's Disorder, immune disorders, and hematopoietic disorders, and the various dyslipidemias, metabolic disturbances associated with obesity, the metabolic syndrome X and wasting disorders associated with chronic diseases and various cancers. The invention also provides for prognostic (or predictive) assays for determining whether an individual is at risk of developing a disorder associated with NOVX protein, nucleic acid expression or activity. For example, mutations in an NOVX gene can be assayed in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with NOVX protein, nucleic acid expression, or biological activity.

Another aspect of the invention provides methods for determining NOVX protein, nucleic acid expression or activity in an individual to thereby select appropriate therapeutic or prophylactic agents for that individual (referred to herein as "pharmacogenomics"). Pharmacogenomics allows for the selection of agents (*e.g.*, drugs) for therapeutic or prophylactic treatment of an individual based on the genotype of the individual (*e.g.*, the genotype of the individual examined to determine the ability of the individual to respond to a particular agent.)

Yet another aspect of the invention pertains to monitoring the influence of agents (*e.g.*, drugs, compounds) on the expression or activity of NOVX in clinical trials.

These and other agents are described in further detail in the following sections.

Diagnostic Assays

An exemplary method for detecting the presence or absence of NOVX in a biological sample involves obtaining a biological sample from a test subject and contacting the biological

sample with a compound or an agent capable of detecting NOVX protein or nucleic acid (*e.g.*, mRNA, genomic DNA) that encodes NOVX protein such that the presence of NOVX is detected in the biological sample. An agent for detecting NOVX mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to NOVX mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length NOVX nucleic acid, such as the nucleic acid of SEQ ID NOS:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, and 31, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to NOVX mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

An agent for detecting NOVX protein is an antibody capable of binding to NOVX protein, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (*e.g.*, Fab or F(ab')₂) can be used. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (*i.e.*, physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently-labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently-labeled streptavidin. The term "biological sample" is intended to include tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. That is, the detection method of the invention can be used to detect NOVX mRNA, protein, or genomic DNA in a biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of NOVX mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of NOVX protein include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations, and immunofluorescence. *In vitro* techniques for detection of NOVX genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of NOVX protein include introducing into a subject a labeled anti-NOVX antibody. For example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

In one embodiment, the biological sample contains protein molecules from the test subject. Alternatively, the biological sample can contain mRNA molecules from the test

subject or genomic DNA molecules from the test subject. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject.

In another embodiment, the methods further involve obtaining a control biological sample from a control subject, contacting the control sample with a compound or agent capable of detecting NOVX protein, mRNA, or genomic DNA, such that the presence of NOVX protein, mRNA or genomic DNA is detected in the biological sample, and comparing the presence of NOVX protein, mRNA or genomic DNA in the control sample with the presence of NOVX protein, mRNA or genomic DNA in the test sample.

The invention also encompasses kits for detecting the presence of NOVX in a biological sample. For example, the kit can comprise: a labeled compound or agent capable of detecting NOVX protein or mRNA in a biological sample; means for determining the amount of NOVX in the sample; and means for comparing the amount of NOVX in the sample with a standard. The compound or agent can be packaged in a suitable container. The kit can further comprise instructions for using the kit to detect NOVX protein or nucleic acid.

Prognostic Assays

The diagnostic methods described herein can furthermore be utilized to identify subjects having or at risk of developing a disease or disorder associated with aberrant NOVX expression or activity. For example, the assays described herein, such as the preceding diagnostic assays or the following assays, can be utilized to identify a subject having or at risk of developing a disorder associated with NOVX protein, nucleic acid expression or activity. Alternatively, the prognostic assays can be utilized to identify a subject having or at risk for developing a disease or disorder. Thus, the invention provides a method for identifying a disease or disorder associated with aberrant NOVX expression or activity in which a test sample is obtained from a subject and NOVX protein or nucleic acid (*e.g.*, mRNA, genomic DNA) is detected, wherein the presence of NOVX protein or nucleic acid is diagnostic for a subject having or at risk of developing a disease or disorder associated with aberrant NOVX expression or activity. As used herein, a "test sample" refers to a biological sample obtained from a subject of interest. For example, a test sample can be a biological fluid (*e.g.*, serum), cell sample, or tissue.

Furthermore, the prognostic assays described herein can be used to determine whether a subject can be administered an agent (*e.g.*, an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) to treat a disease or disorder associated with aberrant NOVX expression or activity. For example, such methods can be

used to determine whether a subject can be effectively treated with an agent for a disorder. Thus, the invention provides methods for determining whether a subject can be effectively treated with an agent for a disorder associated with aberrant NOVX expression or activity in which a test sample is obtained and NOVX protein or nucleic acid is detected (*e.g.*, wherein the presence of NOVX protein or nucleic acid is diagnostic for a subject that can be administered the agent to treat a disorder associated with aberrant NOVX expression or activity).

The methods of the invention can also be used to detect genetic lesions in an NOVX gene, thereby determining if a subject with the lesioned gene is at risk for a disorder characterized by aberrant cell proliferation and/or differentiation. In various embodiments, the methods include detecting, in a sample of cells from the subject, the presence or absence of a genetic lesion characterized by at least one of an alteration affecting the integrity of a gene encoding an NOVX-protein, or the misexpression of the NOVX gene. For example, such genetic lesions can be detected by ascertaining the existence of at least one of: (i) a deletion of one or more nucleotides from an NOVX gene; (ii) an addition of one or more nucleotides to an NOVX gene; (iii) a substitution of one or more nucleotides of an NOVX gene, (iv) a chromosomal rearrangement of an NOVX gene; (v) an alteration in the level of a messenger RNA transcript of an NOVX gene, (vi) aberrant modification of an NOVX gene, such as of the methylation pattern of the genomic DNA, (vii) the presence of a non-wild-type splicing pattern of a messenger RNA transcript of an NOVX gene, (viii) a non-wild-type level of an NOVX protein, (ix) allelic loss of an NOVX gene, and (x) inappropriate post-translational modification of an NOVX protein. As described herein, there are a large number of assay techniques known in the art which can be used for detecting lesions in an NOVX gene. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject. However, any biological sample containing nucleated cells may be used, including, for example, buccal mucosal cells.

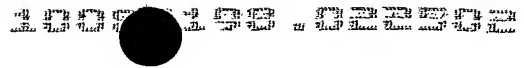
In certain embodiments, detection of the lesion involves the use of a probe/primer in a polymerase chain reaction (PCR) (*see, e.g.*, U.S. Patent Nos. 4,683,195 and 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (*see, e.g.*, Landegran, *et al.*, 1988. *Science* 241: 1077-1080; and Nakazawa, *et al.*, 1994. *Proc. Natl. Acad. Sci. USA* 91: 360-364), the latter of which can be particularly useful for detecting point mutations in the NOVX-gene (*see, Abravaya, et al.*, 1995. *Nucl. Acids Res.* 23: 675-682). This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (*e.g.*, genomic, mRNA or both) from the cells of the sample, contacting the

nucleic acid sample with one or more primers that specifically hybridize to an NOVX gene under conditions such that hybridization and amplification of the NOVX gene (if present) occurs, and detecting the presence or absence of an amplification product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations described herein.

Alternative amplification methods include: self sustained sequence replication (*see*, Guatelli, *et al.*, 1990. *Proc. Natl. Acad. Sci. USA* 87: 1874-1878), transcriptional amplification system (*see*, Kwok, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA* 86: 1173-1177); Q β Replicase (*see*, Lizardi, *et al.*, 1988. *BioTechnology* 6: 1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

In an alternative embodiment, mutations in an NOVX gene from a sample cell can be identified by alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis and compared. Differences in fragment length sizes between sample and control DNA indicates mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (*see, e.g.*, U.S. Patent No. 5,493,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

In other embodiments, genetic mutations in NOVX can be identified by hybridizing a sample and control nucleic acids, *e.g.*, DNA or RNA, to high-density arrays containing hundreds or thousands of oligonucleotide probes. *See, e.g.*, Cronin, *et al.*, 1996. *Human Mutation* 7: 244-255; Kozal, *et al.*, 1996. *Nat. Med.* 2: 753-759. For example, genetic mutations in NOVX can be identified in two dimensional arrays containing light-generated DNA probes as described in Cronin, *et al.*, *supra*. Briefly, a first hybridization array of probes can be used to scan through long stretches of DNA in a sample and control to identify base changes between the sequences by making linear arrays of sequential overlapping probes. This step allows the identification of point mutations. This is followed by a second hybridization array that allows the characterization of specific mutations by using smaller, specialized probe arrays complementary to all variants or mutations detected. Each mutation array is composed of parallel probe sets, one complementary to the wild-type gene and the other complementary to the mutant gene.

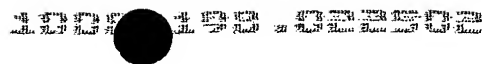


In yet another embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence the NOVX gene and detect mutations by comparing the sequence of the sample NOVX with the corresponding wild-type (control) sequence.

Examples of sequencing reactions include those based on techniques developed by Maxim and Gilbert, 1977. *Proc. Natl. Acad. Sci. USA* 74: 560 or Sanger, 1977. *Proc. Natl. Acad. Sci. USA* 74: 5463. It is also contemplated that any of a variety of automated sequencing procedures can be utilized when performing the diagnostic assays (see, e.g., Naeve, *et al.*, 1995. *Biotechniques* 19: 448), including sequencing by mass spectrometry (see, e.g., PCT International Publication No. WO 94/16101; Cohen, *et al.*, 1996. *Adv. Chromatography* 36: 127-162; and Griffin, *et al.*, 1993. *Appl. Biochem. Biotechnol.* 38: 147-159).

Other methods for detecting mutations in the NOVX gene include methods in which protection from cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA heteroduplexes. See, e.g., Myers, *et al.*, 1985. *Science* 230: 1242. In general, the art technique of "mismatch cleavage" starts by providing heteroduplexes of formed by hybridizing (labeled) RNA or DNA containing the wild-type NOVX sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent that cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and sample strands. For instance, RNA/DNA duplexes can be treated with RNase and DNA/DNA hybrids treated with S₁ nuclease to enzymatically digesting the mismatched regions. In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then separated by size on denaturing polyacrylamide gels to determine the site of mutation. See, e.g., Cotton, *et al.*, 1988. *Proc. Natl. Acad. Sci. USA* 85: 4397; Saleeba, *et al.*, 1992. *Methods Enzymol.* 217: 286-295. In an embodiment, the control DNA or RNA can be labeled for detection.

In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize mismatched base pairs in double-stranded DNA (so called "DNA mismatch repair" enzymes) in defined systems for detecting and mapping point mutations in NOVX cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the thymidine DNA glycosylase from HeLa cells cleaves T at G/T mismatches. See, e.g., Hsu, *et al.*, 1994. *Carcinogenesis* 15: 1657-1662. According to an exemplary embodiment, a probe based on an NOVX sequence, e.g., a wild-type NOVX sequence, is hybridized to a cDNA or other DNA product from a test cell(s). The duplex is



treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. *See, e.g.*, U.S. Patent No. 5,459,039.

In other embodiments, alterations in electrophoretic mobility will be used to identify mutations in NOVX genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type nucleic acids. *See, e.g.*, Orita, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA*: 86: 2766; Cotton, 1993. *Mutat. Res.* 285: 125-144; Hayashi, 1992. *Genet. Anal. Tech. Appl.* 9: 73-79.

Single-stranded DNA fragments of sample and control NOVX nucleic acids will be denatured and allowed to renature. The secondary structure of single-stranded nucleic acids varies according to sequence, the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by using RNA (rather than DNA), in which the secondary structure is more sensitive to a change in sequence. In one embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in electrophoretic mobility. *See, e.g.*, Keen, *et al.*, 1991. *Trends Genet.* 7: 5.

In yet another embodiment, the movement of mutant or wild-type fragments in polyacrylamide gels containing a gradient of denaturant is assayed using denaturing gradient gel electrophoresis (DGGE). *See, e.g.*, Myers, *et al.*, 1985. *Nature* 313: 495. When DGGE is used as the method of analysis, DNA will be modified to insure that it does not completely denature, for example by adding a GC clamp of approximately 40 bp of high-melting GC-rich DNA by PCR. In a further embodiment, a temperature gradient is used in place of a denaturing gradient to identify differences in the mobility of control and sample DNA. *See, e.g.*, Rosenbaum and Reissner, 1987. *Biophys. Chem.* 265: 12753.

Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension. For example, oligonucleotide primers may be prepared in which the known mutation is placed centrally and then hybridized to target DNA under conditions that permit hybridization only if a perfect match is found. *See, e.g.*, Saiki, *et al.*, 1986. *Nature* 324: 163; Saiki, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA* 86: 6230. Such allele specific oligonucleotides are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached to the hybridizing membrane and hybridized with labeled target DNA.

Alternatively, allele specific amplification technology that depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on differential hybridization; *see, e.g., Gibbs, et al., 1989. Nucl. Acids Res. 17: 2437-2448*) or at the extreme 3'-terminus of one primer where, under appropriate conditions, mismatch can prevent, or reduce polymerase extension (*see, e.g., Prossner, 1993. Tibtech. 11: 238*). In addition it may be desirable to introduce a novel restriction site in the region of the mutation to create cleavage-based detection. *See, e.g., Gasparini, et al., 1992. Mol. Cell Probes 6: 1*. It is anticipated that in certain embodiments amplification may also be performed using *Taq* ligase for amplification. *See, e.g., Barany, 1991. Proc. Natl. Acad. Sci. USA 88: 189*. In such cases, ligation will occur only if there is a perfect match at the 3'-terminus of the 5' sequence, making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of amplification.

The methods described herein may be performed, for example, by utilizing pre-packaged diagnostic kits comprising at least one probe nucleic acid or antibody reagent described herein, which may be conveniently used, *e.g.,* in clinical settings to diagnose patients exhibiting symptoms or family history of a disease or illness involving an NOVX gene.

Furthermore, any cell type or tissue, preferably peripheral blood leukocytes, in which NOVX is expressed may be utilized in the prognostic assays described herein. However, any biological sample containing nucleated cells may be used, including, for example, buccal mucosal cells.

Pharmacogenomics

Agents, or modulators that have a stimulatory or inhibitory effect on NOVX activity (*e.g.,* NOVX gene expression), as identified by a screening assay described herein can be administered to individuals to treat (prophylactically or therapeutically) disorders (The disorders include metabolic disorders, diabetes, obesity, infectious disease, anorexia, cancer-associated cachexia, cancer, neurodegenerative disorders, Alzheimer's Disease, Parkinson's Disorder, immune disorders, and hematopoietic disorders, and the various dyslipidemias, metabolic disturbances associated with obesity, the metabolic syndrome X and wasting disorders associated with chronic diseases and various cancers.) In conjunction with such treatment, the pharmacogenomics (*i.e.,* the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may

be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (*e.g.*, drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the activity of NOVX protein, expression of NOVX nucleic acid, or mutation content of NOVX genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See *e.g.*, Eichelbaum, 1996. *Clin. Exp. Pharmacol. Physiol.*, 23: 983-985; Linder, 1997. *Clin. Chem.*, 43: 254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body (altered drug action) or genetic conditions transmitted as single factors altering the way the body acts on drugs (altered drug metabolism). These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common inherited enzymopathy in which the main clinical complication is hemolysis after ingestion of oxidant drugs (anti-malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (*e.g.*, N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, PM show no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. At the other extreme are the so called ultra-rapid

metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the activity of NOVX protein, expression of NOVX nucleic acid, or mutation content of NOVX genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with an NOVX modulator, such as a modulator identified by one of the exemplary screening assays described herein.

Monitoring of Effects During Clinical Trials

Monitoring the influence of agents (*e.g.*, drugs, compounds) on the expression or activity of NOVX (*e.g.*, the ability to modulate aberrant cell proliferation and/or differentiation) can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent determined by a screening assay as described herein to increase NOVX gene expression, protein levels, or upregulate NOVX activity, can be monitored in clinical trials of subjects exhibiting decreased NOVX gene expression, protein levels, or downregulated NOVX activity. Alternatively, the effectiveness of an agent determined by a screening assay to decrease NOVX gene expression, protein levels, or downregulate NOVX activity, can be monitored in clinical trials of subjects exhibiting increased NOVX gene expression, protein levels, or upregulated NOVX activity. In such clinical trials, the expression or activity of NOVX and, preferably, other genes that have been implicated in, for example, a cellular proliferation or immune disorder can be used as a "read out" or markers of the immune responsiveness of a particular cell.

By way of example, and not of limitation, genes, including NOVX, that are modulated in cells by treatment with an agent (*e.g.*, compound, drug or small molecule) that modulates NOVX activity (*e.g.*, identified in a screening assay as described herein) can be identified. Thus, to study the effect of agents on cellular proliferation disorders, for example, in a clinical trial, cells can be isolated and RNA prepared and analyzed for the levels of expression of NOVX and other genes implicated in the disorder. The levels of gene expression (*i.e.*, a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as described herein, or alternatively by measuring the amount of protein produced, by one of the methods

as described herein, or by measuring the levels of activity of NOVX or other genes. In this manner, the gene expression pattern can serve as a marker, indicative of the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

5 In one embodiment, the invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (*e.g.*, an agonist, antagonist, protein, peptide, peptidomimetic, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) comprising the steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression
10 of an NOVX protein, mRNA, or genomic DNA in the preadministration sample; (iii) obtaining one or more post-administration samples from the subject; (iv) detecting the level of expression or activity of the NOVX protein, mRNA, or genomic DNA in the post-administration samples; (v) comparing the level of expression or activity of the NOVX protein, mRNA, or genomic DNA in the pre-administration sample with the NOVX protein,
15 mRNA, or genomic DNA in the post administration sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or activity of NOVX to higher levels than detected, *i.e.*, to increase the effectiveness of the agent. Alternatively, decreased administration of the agent may be desirable to decrease expression or activity of NOVX to
20 lower levels than detected, *i.e.*, to decrease the effectiveness of the agent.

Methods of Treatment

The invention provides for both prophylactic and therapeutic methods of treating a subject at risk of (or susceptible to) a disorder or having a disorder associated with aberrant NOVX expression or activity. The disorders include cardiomyopathy, atherosclerosis,
25 hypertension, congenital heart defects, aortic stenosis, atrial septal defect (ASD), atrioventricular (A-V) canal defect, ductus arteriosus, pulmonary stenosis, subaortic stenosis, ventricular septal defect (VSD), valve diseases, tuberous sclerosis, scleroderma, obesity, transplantation, adrenoleukodystrophy, congenital adrenal hyperplasia, prostate cancer, neoplasm; adenocarcinoma, lymphoma, uterus cancer, fertility, hemophilia, hypercoagulation,
30 idiopathic thrombocytopenic purpura, immunodeficiencies, graft versus host disease, AIDS, bronchial asthma, Crohn's disease; multiple sclerosis, treatment of Albright Hereditary Osteodystrophy, and other diseases, disorders and conditions of the like.

These methods of treatment will be discussed more fully, below.

Disease and Disorders

Diseases and disorders that are characterized by increased (relative to a subject not suffering from the disease or disorder) levels or biological activity may be treated with
 5 Therapeutics that antagonize (*i.e.*, reduce or inhibit) activity. Therapeutics that antagonize activity may be administered in a therapeutic or prophylactic manner. Therapeutics that may be utilized include, but are not limited to: (*i*) an aforementioned peptide, or analogs, derivatives, fragments or homologs thereof; (*ii*) antibodies to an aforementioned peptide; (*iii*) nucleic acids encoding an aforementioned peptide; (*iv*) administration of antisense nucleic acid
 10 and nucleic acids that are “dysfunctional” (*i.e.*, due to a heterologous insertion within the coding sequences of coding sequences to an aforementioned peptide) that are utilized to “knockout” endogenous function of an aforementioned peptide by homologous recombination (*see, e.g.*, Capecchi, 1989. *Science* 244: 1288-1292); or (*v*) modulators (*i.e.*, inhibitors, agonists and antagonists, including additional peptide mimetic of the invention or antibodies
 15 specific to a peptide of the invention) that alter the interaction between an aforementioned peptide and its binding partner.

Diseases and disorders that are characterized by decreased (relative to a subject not suffering from the disease or disorder) levels or biological activity may be treated with
 20 Therapeutics that increase (*i.e.*, are agonists to) activity. Therapeutics that upregulate activity may be administered in a therapeutic or prophylactic manner. Therapeutics that may be utilized include, but are not limited to, an aforementioned peptide, or analogs, derivatives, fragments or homologs thereof; or an agonist that increases bioavailability.

Increased or decreased levels can be readily detected by quantifying peptide and/or RNA, by obtaining a patient tissue sample (*e.g.*, from biopsy tissue) and assaying it *in vitro* for
 25 RNA or peptide levels, structure and/or activity of the expressed peptides (or mRNAs of an aforementioned peptide). Methods that are well-known within the art include, but are not limited to, immunoassays (*e.g.*, by Western blot analysis, immunoprecipitation followed by sodium dodecyl sulfate (SDS) polyacrylamide gel electrophoresis, immunocytochemistry, etc.) and/or hybridization assays to detect expression of mRNAs (*e.g.*, Northern assays, dot blots, *in situ* hybridization, and the like).
 30

Prophylactic Methods

In one aspect, the invention provides a method for preventing, in a subject, a disease or condition associated with an aberrant NOVX expression or activity, by administering to the

subject an agent that modulates NOVX expression or at least one NOVX activity. Subjects at risk for a disease that is caused or contributed to by aberrant NOVX expression or activity can be identified by, for example, any or a combination of diagnostic or prognostic assays as described herein. Administration of a prophylactic agent can occur prior to the manifestation of symptoms characteristic of the NOVX aberrancy, such that a disease or disorder is prevented or, alternatively, delayed in its progression. Depending upon the type of NOVX aberrancy, for example, an NOVX agonist or NOVX antagonist agent can be used for treating the subject. The appropriate agent can be determined based on screening assays described herein. The prophylactic methods of the invention are further discussed in the following subsections.

Therapeutic Methods

Another aspect of the invention pertains to methods of modulating NOVX expression or activity for therapeutic purposes. The modulatory method of the invention involves contacting a cell with an agent that modulates one or more of the activities of NOVX protein activity associated with the cell. An agent that modulates NOVX protein activity can be an agent as described herein, such as a nucleic acid or a protein, a naturally-occurring cognate ligand of an NOVX protein, a peptide, an NOVX peptidomimetic, or other small molecule. In one embodiment, the agent stimulates one or more NOVX protein activity. Examples of such stimulatory agents include active NOVX protein and a nucleic acid molecule encoding NOVX that has been introduced into the cell. In another embodiment, the agent inhibits one or more NOVX protein activity. Examples of such inhibitory agents include antisense NOVX nucleic acid molecules and anti-NOVX antibodies. These modulatory methods can be performed *in vitro* (*e.g.*, by culturing the cell with the agent) or, alternatively, *in vivo* (*e.g.*, by administering the agent to a subject). As such, the invention provides methods of treating an individual afflicted with a disease or disorder characterized by aberrant expression or activity of an NOVX protein or nucleic acid molecule. In one embodiment, the method involves administering an agent (*e.g.*, an agent identified by a screening assay described herein), or combination of agents that modulates (*e.g.*, up-regulates or down-regulates) NOVX expression or activity. In another embodiment, the method involves administering an NOVX protein or nucleic acid molecule as therapy to compensate for reduced or aberrant NOVX expression or activity.

Stimulation of NOVX activity is desirable *in situations* in which NOVX is abnormally downregulated and/or in which increased NOVX activity is likely to have a beneficial effect.

One example of such a situation is where a subject has a disorder characterized by aberrant cell proliferation and/or differentiation (*e.g.*, cancer or immune associated disorders). Another example of such a situation is where the subject has a gestational disease (*e.g.*, preeclampsia).

Determination of the Biological Effect of the Therapeutic

5 In various embodiments of the invention, suitable *in vitro* or *in vivo* assays are performed to determine the effect of a specific Therapeutic and whether its administration is indicated for treatment of the affected tissue.

In various specific embodiments, *in vitro* assays may be performed with representative cells of the type(s) involved in the patient's disorder, to determine if a given Therapeutic exerts the desired effect upon the cell type(s). Compounds for use in therapy may be tested in suitable animal model systems including, but not limited to rats, mice, chicken, cows, monkeys, rabbits, and the like, prior to testing in human subjects. Similarly, for *in vivo* testing, any of the animal model system known in the art may be used prior to administration to human subjects.

15 Prophylactic and Therapeutic Uses of the Compositions of the Invention

The NOVX nucleic acids and proteins of the invention are useful in potential prophylactic and therapeutic applications implicated in a variety of disorders including, but not limited to: metabolic disorders, diabetes, obesity, infectious disease, anorexia, cancer-associated cancer, neurodegenerative disorders, Alzheimer's Disease, Parkinson's Disorder, immune disorders, hematopoietic disorders, and the various dyslipidemias, metabolic disturbances associated with obesity, the metabolic syndrome X and wasting disorders associated with chronic diseases and various cancers.

As an example, a cDNA encoding the NOVX protein of the invention may be useful in gene therapy, and the protein may be useful when administered to a subject in need thereof.

25 By way of non-limiting example, the compositions of the invention will have efficacy for treatment of patients suffering from: metabolic disorders, diabetes, obesity, infectious disease, anorexia, cancer-associated cachexia, cancer, neurodegenerative disorders, Alzheimer's Disease, Parkinson's Disorder, immune disorders, hematopoietic disorders, and the various dyslipidemias.

Both the novel nucleic acid encoding the NOVX protein, and the NOVX protein of the invention, or fragments thereof, may also be useful in diagnostic applications, wherein the presence or amount of the nucleic acid or the protein are to be assessed. A further use could be as an anti-bacterial molecule (*i.e.*, some peptides have been found to possess anti-bacterial

properties). These materials are further useful in the generation of antibodies, which immunospecifically-bind to the novel substances of the invention for use in therapeutic or diagnostic methods.

The invention will be further described in the following examples, which do not limit
5 the scope of the invention described in the claims.

Examples

Example 1. Identification of NOVX clones

The novel NOVX target sequences identified in the present invention were subjected to
10 the exon linking process to confirm the sequence. PCR primers were designed by starting at the most upstream sequence available, for the forward primer, and at the most downstream sequence available for the reverse primer. Table 13A shows the sequences of the PCR primers used for obtaining different clones. In each case, the sequence was examined, walking inward from the respective termini toward the coding sequence, until a suitable sequence that is either
15 unique or highly selective was encountered, or, in the case of the reverse primer, until the stop codon was reached. Such primers were designed based on in silico predictions for the full length cDNA, part (one or more exons) of the DNA or protein sequence of the target sequence, or by translated homology of the predicted exons to closely related human sequences from other species. These primers were then employed in PCR amplification based
20 on the following pool of human cDNAs: adrenal gland, bone marrow, brain - amygdala, brain - cerebellum, brain - hippocampus, brain - substantia nigra, brain - thalamus, brain -whole, fetal brain, fetal kidney, fetal liver, fetal lung, heart, kidney, lymphoma - Raji, mammary gland, pancreas, pituitary gland, placenta, prostate, salivary gland, skeletal muscle, small intestine, spinal cord, spleen, stomach, testis, thyroid, trachea, uterus. Usually the resulting
25 amplicons were gel purified, cloned and sequenced to high redundancy. The PCR product derived from exon linking was cloned into the pCR2.1 vector from Invitrogen. The resulting bacterial clone has an insert covering the entire open reading frame cloned into the pCR2.1 vector. Table 13B shows a list of these bacterial clones. The resulting sequences from all clones were assembled with themselves, with other fragments in CuraGen Corporation's
30 database and with public ESTs. Fragments and ESTs were included as components for an assembly when the extent of their identity with another component of the assembly was at least 95% over 50 bp. In addition, sequence traces were evaluated manually and edited for corrections if appropriate. These procedures provide the sequence reported herein.

Table EL1A. PCR Primers for Exon Linking

NOVX Clone	Primer 1 (5' - 3')	SEQ ID NO	Primer 2 (5' - 3')	SEQ ID NO
4b	GAAGGTTTCCCTGGGCGTTCCTT	215	GTGAGGTGCAGGCAAAACCAATGATT	216
15	GACCCCAAGAGCCTTAATGACTCTAGA	217	CTGTCCGTCGTCCTTCAGAGTCAT	218
21	CAACCAAGAGGCAAGAGG	219	CTCCATGAGACTCAGTGAATAAGA	220
23	CTGCCTTCTGCCTTATGCCA	221	TTAAGTTCTAGGGTACATGTGCACAAC	222
24	GCCTGGTCTCTGCTGACTG	223	CCGCATCAGCCTAGGGGTACTAGAGAT	224
42b	CTGTGCACTGTTGGTGGGAATATAAAA	225	TCTGGTGGTTAAGATAAAACACAAGTCA	226
47	TTCGGCTGCTGCTGACCAT	227	CCTGGTAGCCTCAAAGCTTCTTAGTTC	228
57	ATGGCTGCCGAGAACTCCTCCTC	229	TCAAGAAAAGCTTATTCTGGAAGGTTCTCTTC	230
58	AACCCCTGCTGTCATCCTTCTC	231	GCTACAAAAGGTTTCTTTCTGATCTGC	232
60c	GTAAACATTTGGCCAGCTTGGTTTG	233	CAGCTGCCTGGCTAACTCCTATAACAC	234
62b	AAGGTGCTGAAATAGCAATGACAAGAG	235	CAGAGTCTCTCCCTAGCTCCCCAG	236
67b	ATACCCACGTTCCGCTATGAGATT	237	GTGTCACGTCGAGTGGTTGGTG	238
69b	CACATAGTCTTGGCTCCAGTTTCGT	239	CTAAAGTTTATTCCAATCAGTGTTTTTTTT TCC	240
81b	GAATGATGCCCTTTTGCCACAA	241	CTATGAACCAATTCCAAAATAATTTACACCTG	242

Physical clone: Exons were predicted by homology and the intron/exon boundaries were determined using standard genetic rules. Exons were further selected and refined by means of similarity determination using multiple BLAST (for example, tBlastN, BlastX, and BlastN) searches, and, in some instances, GeneScan and Grail. Expressed sequences from both public and proprietary databases were also added when available to further define and complete the gene sequence. The DNA sequence was then manually corrected for apparent inconsistencies thereby obtaining the sequences encoding the full-length protein.

Example 2. Quantitative expression analysis of clones in various tissues and cells

The quantitative expression of various clones was assessed using microtiter plates containing RNA samples from a variety of normal and pathology-derived cells, cell lines and tissues using real time quantitative PCR (RTQ PCR). RTQ PCR was performed on an Applied Biosystems ABI PRISM® 7700 or an ABI PRISM® 7900 HT Sequence Detection System. Various collections of samples are assembled on the plates, and referred to as Panel 1 (containing normal tissues and cancer cell lines), Panel 2 (containing samples derived from tissues from normal and cancer sources), Panel 3 (containing cancer cell lines), Panel 4 (containing cells and cell lines from normal tissues and cells related to inflammatory conditions), Panel 5D/5I (containing human tissues and cell lines with an emphasis on metabolic diseases), AI_comprehensive_panel (containing normal tissue and samples from autoimmune diseases), Panel CNSD.01 (containing central nervous system samples from

normal and diseased brains) and CNS_neurodegeneration_panel (containing samples from normal and Alzheimer's diseased brains).

RNA integrity from all samples is controlled for quality by visual assessment of agarose gel electropherograms using 28S and 18S ribosomal RNA staining intensity ratio as a guide (2:1 to 2.5:1 28s:18s) and the absence of low molecular weight RNAs that would be indicative of degradation products. Samples are controlled against genomic DNA contamination by RTQ PCR reactions run in the absence of reverse transcriptase using probe and primer sets designed to amplify across the span of a single exon.

First, the RNA samples were normalized to reference nucleic acids such as constitutively expressed genes (for example, β -actin and GAPDH). Normalized RNA (5 μ l) was converted to cDNA and analyzed by RTQ-PCR using One Step RT-PCR Master Mix Reagents (Applied Biosystems; Catalog No. 4309169) and gene-specific primers according to the manufacturer's instructions.

In other cases, non-normalized RNA samples were converted to single strand cDNA (sscDNA) using Superscript II (Invitrogen Corporation; Catalog No. 18064-147) and random hexamers according to the manufacturer's instructions. Reactions containing up to 10 μ g of total RNA were performed in a volume of 20 μ l and incubated for 60 minutes at 42°C. This reaction can be scaled up to 50 μ g of total RNA in a final volume of 100 μ l. sscDNA samples are then normalized to reference nucleic acids as described previously, using 1X TaqMan® Universal Master mix (Applied Biosystems; catalog No. 4324020), following the manufacturer's instructions.

Probes and primers were designed for each assay according to Applied Biosystems Primer Express Software package (version I for Apple Computer's Macintosh Power PC) or a similar algorithm using the target sequence as input. Default settings were used for reaction conditions and the following parameters were set before selecting primers: primer concentration = 250 nM, primer melting temperature (T_m) range = 58°-60°C, primer optimal T_m = 59°C, maximum primer difference = 2°C, probe does not have 5'G, probe T_m must be 10°C greater than primer T_m , amplicon size 75bp to 100bp. The probes and primers selected (see below) were synthesized by Synthesgen (Houston, TX, USA). Probes were double purified by HPLC to remove uncoupled dye and evaluated by mass spectroscopy to verify coupling of reporter and quencher dyes to the 5' and 3' ends of the probe, respectively. Their final concentrations were: forward and reverse primers, 900nM each, and probe, 200nM.

PCR conditions: When working with RNA samples, normalized RNA from each tissue and each cell line was spotted in each well of either a 96 well or a 384-well PCR plate (Applied Biosystems). PCR cocktails included either a single gene specific probe and primers set, or two multiplexed probe and primers sets (a set specific for the target clone and another gene-specific set multiplexed with the target probe). PCR reactions were set up using TaqMan® One-Step RT-PCR Master Mix (Applied Biosystems, Catalog No. 4313803) following manufacturer's instructions. Reverse transcription was performed at 48°C for 30 minutes followed by amplification/PCR cycles as follows: 95°C 10 min, then 40 cycles of 95°C for 15 seconds, 60°C for 1 minute. Results were recorded as CT values (cycle at which a given sample crosses a threshold level of fluorescence) using a log scale, with the difference in RNA concentration between a given sample and the sample with the lowest CT value being represented as 2 to the power of delta CT. The percent relative expression is then obtained by taking the reciprocal of this RNA difference and multiplying by 100.

When working with sscDNA samples, normalized sscDNA was used as described previously for RNA samples. PCR reactions containing one or two sets of probe and primers were set up as described previously, using 1X TaqMan® Universal Master mix (Applied Biosystems; catalog No. 4324020), following the manufacturer's instructions. PCR amplification was performed as follows: 95°C 10 min, then 40 cycles of 95°C for 15 seconds, 60°C for 1 minute. Results were analyzed and processed as described previously.

Panels 1, 1.1, 1.2, and 1.3D

The plates for Panels 1, 1.1, 1.2 and 1.3D include 2 control wells (genomic DNA control and chemistry control) and 94 wells containing cDNA from various samples. The samples in these panels are broken into 2 classes: samples derived from cultured cell lines and samples derived from primary normal tissues. The cell lines are derived from cancers of the following types: lung cancer, breast cancer, melanoma, colon cancer, prostate cancer, CNS cancer, squamous cell carcinoma, ovarian cancer, liver cancer, renal cancer, gastric cancer and pancreatic cancer. Cell lines used in these panels are widely available through the American Type Culture Collection (ATCC), a repository for cultured cell lines, and were cultured using the conditions recommended by the ATCC. The normal tissues found on these panels are comprised of samples derived from all major organ systems from single adult individuals or fetuses. These samples are derived from the following organs: adult skeletal muscle, fetal skeletal muscle, adult heart, fetal heart, adult kidney, fetal kidney, adult liver, fetal liver, adult lung, fetal lung, various regions of the brain, the spleen, bone marrow, lymph node, pancreas,

salivary gland, pituitary gland, adrenal gland, spinal cord, thymus, stomach, small intestine, colon, bladder, trachea, breast, ovary, uterus, placenta, prostate, testis and adipose.

In the results for Panels 1, 1.1, 1.2 and 1.3D, the following abbreviations are used:

ca. = carcinoma,

* = established from metastasis,

met = metastasis,

s cell var = small cell variant,

non-s = non-sm = non-small,

squam = squamous,

pl. eff = pl effusion = pleural effusion,

glio = glioma,

astro = astrocytoma, and

neuro = neuroblastoma.

General_screening_panel_v1.4

The plates for Panel 1.4 include 2 control wells (genomic DNA control and chemistry control) and 94 wells containing cDNA from various samples. The samples in Panel 1.4 are broken into 2 classes: samples derived from cultured cell lines and samples derived from primary normal tissues. The cell lines are derived from cancers of the following types: lung cancer, breast cancer, melanoma, colon cancer, prostate cancer, CNS cancer, squamous cell carcinoma, ovarian cancer, liver cancer, renal cancer, gastric cancer and pancreatic cancer. Cell lines used in Panel 1.4 are widely available through the American Type Culture Collection (ATCC), a repository for cultured cell lines, and were cultured using the conditions recommended by the ATCC. The normal tissues found on Panel 1.4 are comprised of pools of samples derived from all major organ systems from 2 to 5 different adult individuals or fetuses. These samples are derived from the following organs: adult skeletal muscle, fetal skeletal muscle, adult heart, fetal heart, adult kidney, fetal kidney, adult liver, fetal liver, adult lung, fetal lung, various regions of the brain, the spleen, bone marrow, lymph node, pancreas, salivary gland, pituitary gland, adrenal gland, spinal cord, thymus, stomach, small intestine, colon, bladder, trachea, breast, ovary, uterus, placenta, prostate, testis and adipose.

Abbreviations are as described for Panels 1, 1.1, 1.2, and 1.3D.

Panels 2D and 2.2

The plates for Panels 2D and 2.2 generally include 2 control wells and 94 test samples composed of RNA or cDNA isolated from human tissue procured by surgeons working in

close cooperation with the National Cancer Institute's Cooperative Human Tissue Network (CHTN) or the National Disease Research Initiative (NDRI). The tissues are derived from human malignancies and in cases where indicated many malignant tissues have "matched margins" obtained from noncancerous tissue just adjacent to the tumor. These are termed normal adjacent tissues and are denoted "NAT" in the results below. The tumor tissue and the "matched margins" are evaluated by two independent pathologists (the surgical pathologists and again by a pathologist at NDRI or CHTN). This analysis provides a gross histopathological assessment of tumor differentiation grade. Moreover, most samples include the original surgical pathology report that provides information regarding the clinical stage of the patient. These matched margins are taken from the tissue surrounding (i.e. immediately proximal) to the zone of surgery (designated "NAT", for normal adjacent tissue, in Table RR). In addition, RNA and cDNA samples were obtained from various human tissues derived from autopsies performed on elderly people or sudden death victims (accidents, etc.). These tissues were ascertained to be free of disease and were purchased from various commercial sources such as Clontech (Palo Alto, CA), Research Genetics, and Invitrogen.

Panel 3D

The plates of Panel 3D are comprised of 94 cDNA samples and two control samples. Specifically, 92 of these samples are derived from cultured human cancer cell lines, 2 samples of human primary cerebellar tissue and 2 controls. The human cell lines are generally obtained from ATCC (American Type Culture Collection), NCI or the German tumor cell bank and fall into the following tissue groups: Squamous cell carcinoma of the tongue, breast cancer, prostate cancer, melanoma, epidermoid carcinoma, sarcomas, bladder carcinomas, pancreatic cancers, kidney cancers, leukemias/lymphomas, ovarian/uterine/cervical, gastric, colon, lung and CNS cancer cell lines. In addition, there are two independent samples of cerebellum. These cells are all cultured under standard recommended conditions and RNA extracted using the standard procedures. The cell lines in panel 3D and 1.3D are of the most common cell lines used in the scientific literature.

Panels 4D, 4R, and 4.1D

Panel 4 includes samples on a 96 well plate (2 control wells, 94 test samples) composed of RNA (Panel 4R) or cDNA (Panels 4D/4.1D) isolated from various human cell lines or tissues related to inflammatory conditions. Total RNA from control normal tissues such as colon and lung (Stratagene, La Jolla, CA) and thymus and kidney (Clontech) was employed. Total RNA from liver tissue from cirrhosis patients and kidney from lupus patients

was obtained from BioChain (Biochain Institute, Inc., Hayward, CA). Intestinal tissue for RNA preparation from patients diagnosed as having Crohn's disease and ulcerative colitis was obtained from the National Disease Research Interchange (NDRI) (Philadelphia, PA).

5 Astrocytes, lung fibroblasts, dermal fibroblasts, coronary artery smooth muscle cells, small airway epithelium, bronchial epithelium, microvascular dermal endothelial cells, microvascular lung endothelial cells, human pulmonary aortic endothelial cells, human umbilical vein endothelial cells were all purchased from Clonetics (Walkersville, MD) and grown in the media supplied for these cell types by Clonetics. These primary cell types were activated with various cytokines or combinations of cytokines for 6 and/or 12-14 hours, as indicated. The following cytokines were used; IL-1 beta at approximately 1-5ng/ml, TNF alpha at approximately 5-10ng/ml, IFN gamma at approximately 20-50ng/ml, IL-4 at approximately 5-10ng/ml, IL-9 at approximately 5-10ng/ml, IL-13 at approximately 5-10ng/ml. Endothelial cells were sometimes starved for various times by culture in the basal media from Clonetics with 0.1% serum.

15 Mononuclear cells were prepared from blood of employees at CuraGen Corporation, using Ficoll. LAK cells were prepared from these cells by culture in DMEM 5% FCS (Hyclone), 100μM non essential amino acids (Gibco/Life Technologies, Rockville, MD), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10mM Hepes (Gibco) and Interleukin 2 for 4-6 days. Cells were then either activated with 10-20ng/ml PMA and 1-2μg/ml ionomycin, IL-12 at 5-10ng/ml, IFN gamma at 20-50ng/ml and IL-18 at 5-10ng/ml for 6 hours. In some cases, mononuclear cells were cultured for 4-5 days in DMEM 5% FCS (Hyclone), 100μM non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10mM Hepes (Gibco) with PHA (phytohemagglutinin) or PWM (pokeweed mitogen) at approximately 5μg/ml. Samples were taken at 24, 48 and 72 hours for RNA preparation. MLR (mixed lymphocyte reaction) samples were obtained by taking blood from two donors, isolating the mononuclear cells using Ficoll and mixing the isolated mononuclear cells 1:1 at a final concentration of approximately 2×10^6 cells/ml in DMEM 5% FCS (Hyclone), 100μM non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol (5.5×10^{-5} M) (Gibco), and 10mM Hepes (Gibco). The MLR was cultured and samples taken at various time points ranging from 1- 7 days for RNA preparation.

Monocytes were isolated from mononuclear cells using CD14 Miltenyi Beads, +ve VS selection columns and a Vario Magnet according to the manufacturer's instructions. Monocytes were differentiated into dendritic cells by culture in DMEM 5% fetal calf serum

(FCS) (Hyclone, Logan, UT), 100 μ M non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5x10⁻⁵M (Gibco), and 10mM Hepes (Gibco), 50ng/ml GMCSF and 5ng/ml IL-4 for 5-7 days. Macrophages were prepared by culture of monocytes for 5-7 days in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5x10⁻⁵M (Gibco), 10mM Hepes (Gibco) and 10% AB Human Serum or MCSF at approximately 50ng/ml. Monocytes, macrophages and dendritic cells were stimulated for 6 and 12-14 hours with lipopolysaccharide (LPS) at 100ng/ml. Dendritic cells were also stimulated with anti-CD40 monoclonal antibody (Pharmingen) at 10 μ g/ml for 6 and 12-14 hours.

CD4 lymphocytes, CD8 lymphocytes and NK cells were also isolated from mononuclear cells using CD4, CD8 and CD56 Miltenyi beads, positive VS selection columns and a Vario Magnet according to the manufacturer's instructions. CD45RA and CD45RO CD4 lymphocytes were isolated by depleting mononuclear cells of CD8, CD56, CD14 and CD19 cells using CD8, CD56, CD14 and CD19 Miltenyi beads and positive selection. CD45RO beads were then used to isolate the CD45RO CD4 lymphocytes with the remaining cells being CD45RA CD4 lymphocytes. CD45RA CD4, CD45RO CD4 and CD8 lymphocytes were placed in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5x10⁻⁵M (Gibco), and 10mM Hepes (Gibco) and plated at 10⁶cells/ml onto Falcon 6 well tissue culture plates that had been coated overnight with 0.5 μ g/ml anti-CD28 (Pharmingen) and 3 μ g/ml anti-CD3 (OKT3, ATCC) in PBS. After 6 and 24 hours, the cells were harvested for RNA preparation. To prepare chronically activated CD8 lymphocytes, the isolated CD8 lymphocytes were activated for 4 days on anti-CD28 and anti-CD3 coated plates and then harvested the cells and expanded them in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5x10⁻⁵M (Gibco), and 10mM Hepes (Gibco) and IL-2. The expanded CD8 cells were then activated again with plate bound anti-CD3 and anti-CD28 for 4 days and expanded as before. RNA was isolated 6 and 24 hours after the second activation and after 4 days of the second expansion culture. The isolated NK cells were cultured in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5x10⁻⁵M (Gibco), and 10mM Hepes (Gibco) and IL-2 for 4-6 days before RNA was prepared.

To obtain B cells, tonsils were procured from NDRI. The tonsil was cut up with sterile dissecting scissors and then passed through a sieve. Tonsil cells were then spun down and resuspended at 10⁶cells/ml in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids

(Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10mM Hepes (Gibco). To activate the cells, PWM was used at 5 μ g/ml or anti-CD40 (Pharmingen) at approximately 10 μ g/ml and IL-4 at 5-10ng/ml. Cells were harvested for RNA preparation at 24, 48 and 72 hours.

5 To prepare the primary and secondary Th1/Th2 and Tr1 cells, six-well Falcon plates were coated overnight with 10 μ g/ml anti-CD28 (Pharmingen) and 2 μ g/ml OKT3 (ATCC), and then washed twice with PBS. Umbilical cord blood CD4 lymphocytes (Poietic Systems, German Town, MD) were cultured at 10^5 - 10^6 cells/ml in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), 10mM Hepes (Gibco) and IL-2 (4ng/ml). IL-12 (5ng/ml) and anti-IL4 (1 μ g/ml) were used to direct to Th1, while IL-4 (5ng/ml) and anti-IFN gamma (1 μ g/ml) were used to direct to Th2 and IL-10 at 5ng/ml was used to direct to Tr1. After 4-5 days, the activated Th1, Th2 and Tr1 lymphocytes were washed once in DMEM and expanded for 4-7 days in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), 10mM Hepes (Gibco) and IL-2 (1ng/ml). Following this, the activated Th1, Th2 and Tr1 lymphocytes were re-stimulated for 5 days with anti-CD28/OKT3 and cytokines as described above, but with the addition of anti-CD95L (1 μ g/ml) to prevent apoptosis. After 4-5 days, the Th1, Th2 and Tr1 lymphocytes were washed and then expanded again with IL-2 for 4-7 days. Activated Th1 and Th2 lymphocytes were maintained in this way for a maximum of three cycles. RNA was prepared from primary and secondary Th1, Th2 and Tr1 after 6 and 24 hours following the second and third activations with plate bound anti-CD3 and anti-CD28 mAbs and 4 days into the second and third expansion cultures in Interleukin 2.

25 The following leukocyte cells lines were obtained from the ATCC: Ramos, EOL-1, KU-812. EOL cells were further differentiated by culture in 0.1mM dbcAMP at 5×10^5 cells/ml for 8 days, changing the media every 3 days and adjusting the cell concentration to 5×10^5 cells/ml. For the culture of these cells, DMEM or RPMI (as recommended by the ATCC) was used, with the addition of 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), 10mM Hepes (Gibco). RNA was either prepared from resting cells or cells activated with PMA at 10ng/ml and ionomycin at 1 μ g/ml for 6 and 14 hours. Keratinocyte line CCD106 and an airway epithelial tumor line NCI-H292 were also obtained from the ATCC. Both were cultured in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10mM Hepes (Gibco). CCD1106 cells were

activated for 6 and 14 hours with approximately 5 ng/ml TNF alpha and 1ng/ml IL-1 beta, while NCI-H292 cells were activated for 6 and 14 hours with the following cytokines: 5ng/ml IL-4, 5ng/ml IL-9, 5ng/ml IL-13 and 25ng/ml IFN gamma.

For these cell lines and blood cells, RNA was prepared by lysing approximately 5
 10⁷ cells/ml using Trizol (Gibco BRL). Briefly, 1/10 volume of bromochloropropane (Molecular Research Corporation) was added to the RNA sample, vortexed and after 10 minutes at room temperature, the tubes were spun at 14,000 rpm in a Sorvall SS34 rotor. The aqueous phase was removed and placed in a 15ml Falcon Tube. An equal volume of isopropanol was added and left at -20°C overnight. The precipitated RNA was spun down at 10
 9,000 rpm for 15 min in a Sorvall SS34 rotor and washed in 70% ethanol. The pellet was redissolved in 300µl of RNase-free water and 35µl buffer (Promega) 5µl DTT, 7µl RNAsin and 8µl DNase were added. The tube was incubated at 37°C for 30 minutes to remove contaminating genomic DNA, extracted once with phenol chloroform and re-precipitated with 1/10 volume of 3M sodium acetate and 2 volumes of 100% ethanol. The RNA was spun down 15
 and placed in RNase free water. RNA was stored at -80°C.

AI_comprehensive panel_v1.0

The plates for AI_comprehensive panel_v1.0 include two control wells and 89 test samples comprised of cDNA isolated from surgical and postmortem human tissues obtained from the Backus Hospital and Clinomics (Frederick, MD). Total RNA was extracted from 20
 tissue samples from the Backus Hospital in the Facility at CuraGen. Total RNA from other tissues was obtained from Clinomics.

Joint tissues including synovial fluid, synovium, bone and cartilage were obtained from patients undergoing total knee or hip replacement surgery at the Backus Hospital. Tissue samples were immediately snap frozen in liquid nitrogen to ensure that isolated RNA was of 25
 optimal quality and not degraded. Additional samples of osteoarthritis and rheumatoid arthritis joint tissues were obtained from Clinomics. Normal control tissues were supplied by Clinomics and were obtained during autopsy of trauma victims.

Surgical specimens of psoriatic tissues and adjacent matched tissues were provided as total RNA by Clinomics. Two male and two female patients were selected between the ages of 30
 25 and 47. None of the patients were taking prescription drugs at the time samples were isolated.

Surgical specimens of diseased colon from patients with ulcerative colitis and Crohns disease and adjacent matched tissues were obtained from Clinomics. Bowel tissue from three

female and three male Crohn's patients between the ages of 41-69 were used. Two patients were not on prescription medication while the others were taking dexamethasone, phenobarbital, or tylenol. Ulcerative colitis tissue was from three male and four female patients. Four of the patients were taking lebid and two were on phenobarbital.

5 Total RNA from post mortem lung tissue from trauma victims with no disease or with emphysema, asthma or COPD was purchased from Clinomics. Emphysema patients ranged in age from 40-70 and all were smokers, this age range was chosen to focus on patients with cigarette-linked emphysema and to avoid those patients with alpha-1 anti-trypsin deficiencies. Asthma patients ranged in age from 36-75, and excluded smokers to prevent those patients that
10 could also have COPD. COPD patients ranged in age from 35-80 and included both smokers and non-smokers. Most patients were taking corticosteroids, and bronchodilators.

In the labels employed to identify tissues in the AI_comprehensive panel_v1.0 panel, the following abbreviations are used:

AI = Autoimmunity
15 Syn = Synovial
Normal = No apparent disease
Rep22 /Rep20 = individual patients
RA = Rheumatoid arthritis
Backus = From Backus Hospital
20 OA = Osteoarthritis
(SS) (BA) (MF) = Individual patients
Adj = Adjacent tissue
Match control = adjacent tissues
-M = Male
25 -F = Female
COPD = Chronic obstructive pulmonary disease

Panels 5D and 5I

The plates for Panel 5D and 5I include two control wells and a variety of cDNAs isolated from human tissues and cell lines with an emphasis on metabolic diseases. Metabolic
30 tissues were obtained from patients enrolled in the Gestational Diabetes study. Cells were obtained during different stages in the differentiation of adipocytes from human mesenchymal stem cells. Human pancreatic islets were also obtained.

In the Gestational Diabetes study subjects are young (18 - 40 years), otherwise healthy women with and without gestational diabetes undergoing routine (elective) Caesarean section. After delivery of the infant, when the surgical incisions were being repaired/closed, the obstetrician removed a small sample (<1 cc) of the exposed metabolic tissues during the closure of each surgical level. The biopsy material was rinsed in sterile saline, blotted and fast frozen within 5 minutes from the time of removal. The tissue was then flash frozen in liquid nitrogen and stored, individually, in sterile screw-top tubes and kept on dry ice for shipment to or to be picked up by CuraGen. The metabolic tissues of interest include uterine wall (smooth muscle), visceral adipose, skeletal muscle (rectus) and subcutaneous adipose. Patient descriptions are as follows:

- Patient 2: Diabetic Hispanic, overweight, not on insulin
- Patient 7-9: Nondiabetic Caucasian and obese (BMI>30)
- Patient 10: Diabetic Hispanic, overweight, on insulin
- Patient 11: Nondiabetic African American and overweight
- Patient 12: Diabetic Hispanic on insulin

Adipocyte differentiation was induced in donor progenitor cells obtained from Osirus (a division of Clonetics/BioWhittaker) in triplicate, except for Donor 3U which had only two replicates. Scientists at Clonetics isolated, grew and differentiated human mesenchymal stem cells (HuMSCs) for CuraGen based on the published protocol found in Mark F. Pittenger, et al., Multilineage Potential of Adult Human Mesenchymal Stem Cells Science Apr 2 1999: 143-147. Clonetics provided Trizol lysates or frozen pellets suitable for mRNA isolation and ds cDNA production. A general description of each donor is as follows:

- Donor 2 and 3 U: Mesenchymal Stem cells, Undifferentiated Adipose
- Donor 2 and 3 AM: Adipose, AdiposeMidway Differentiated
- Donor 2 and 3 AD: Adipose, Adipose Differentiated

Human cell lines were generally obtained from ATCC (American Type Culture Collection), NCI or the German tumor cell bank and fall into the following tissue groups: kidney proximal convoluted tubule, uterine smooth muscle cells, small intestine, liver HepG2 cancer cells, heart primary stromal cells, and adrenal cortical adenoma cells. These cells are all cultured under standard recommended conditions and RNA extracted using the standard procedures. All samples were processed at CuraGen to produce single stranded cDNA.

Panel 5I contains all samples previously described with the addition of pancreatic islets from a 58 year old female patient obtained from the Diabetes Research Institute at the University of Miami School of Medicine. Islet tissue was processed to total RNA at an outside source and delivered to CuraGen for addition to panel 5I.

5 In the labels employed to identify tissues in the 5D and 5I panels, the following abbreviations are used:

GO Adipose = Greater Omentum Adipose

SK = Skeletal Muscle

UT = Uterus

10 PL = Placenta

AD = Adipose Differentiated

AM = Adipose Midway Differentiated

U = Undifferentiated Stem Cells

Panel CNSD.01

15 The plates for Panel CNSD.01 include two control wells and 94 test samples comprised of cDNA isolated from postmortem human brain tissue obtained from the Harvard Brain Tissue Resource Center. Brains are removed from calvaria of donors between 4 and 24 hours after death, sectioned by neuroanatomists, and frozen at -80°C in liquid nitrogen vapor. All brains are sectioned and examined by neuropathologists to confirm diagnoses with clear
20 associated neuropathology.

Disease diagnoses are taken from patient records. The panel contains two brains from each of the following diagnoses: Alzheimer's disease, Parkinson's disease, Huntington's disease, Progressive Supranuclear Palsy, Depression, and "Normal controls". Within each of these brains, the following regions are represented: cingulate gyrus, temporal pole, globus
25 pallidus, substantia nigra, Brodman Area 4 (primary motor strip), Brodman Area 7 (parietal cortex), Brodman Area 9 (prefrontal cortex), and Brodman area 17 (occipital cortex). Not all brain regions are represented in all cases; e.g., Huntington's disease is characterized in part by neurodegeneration in the globus pallidus, thus this region is impossible to obtain from confirmed Huntington's cases. Likewise Parkinson's disease is characterized by degeneration
30 of the substantia nigra making this region more difficult to obtain. Normal control brains were examined for neuropathology and found to be free of any pathology consistent with neurodegeneration.

In the labels employed to identify tissues in the CNS panel, the following abbreviations are used:

- PSP = Progressive supranuclear palsy
- Sub Nigra = Substantia nigra
- 5 Glob Palladus= Globus palladus
- Temp Pole = Temporal pole
- Cing Gyr = Cingulate gyrus
- BA 4 = Brodman Area 4

Panel CNS_Neurodegeneration_V1.0

- 10 The plates for Panel CNS_Neurodegeneration_V1.0 include two control wells and 47 test samples comprised of cDNA isolated from postmortem human brain tissue obtained from the Harvard Brain Tissue Resource Center (McLean Hospital) and the Human Brain and Spinal Fluid Resource Center (VA Greater Los Angeles Healthcare System). Brains are removed from calvaria of donors between 4 and 24 hours after death, sectioned by
- 15 neuroanatomists, and frozen at -80°C in liquid nitrogen vapor. All brains are sectioned and examined by neuropathologists to confirm diagnoses with clear associated neuropathology.

- Disease diagnoses are taken from patient records. The panel contains six brains from Alzheimer's disease (AD) patients, and eight brains from "Normal controls" who showed no evidence of dementia prior to death. The eight normal control brains are divided into two
- 20 categories: Controls with no dementia and no Alzheimer's like pathology (Controls) and controls with no dementia but evidence of severe Alzheimer's like pathology, (specifically senile plaque load rated as level 3 on a scale of 0-3; 0 = no evidence of plaques, 3 = severe AD senile plaque load). Within each of these brains, the following regions are represented: hippocampus, temporal cortex (Brodman Area 21), parietal cortex (Brodman area 7), and
- 25 occipital cortex (Brodman area 17). These regions were chosen to encompass all levels of neurodegeneration in AD. The hippocampus is a region of early and severe neuronal loss in AD; the temporal cortex is known to show neurodegeneration in AD after the hippocampus; the parietal cortex shows moderate neuronal death in the late stages of the disease; the occipital cortex is spared in AD and therefore acts as a "control" region within AD patients.
- 30 Not all brain regions are represented in all cases.

In the labels employed to identify tissues in the CNS_Neurodegeneration_V1.0 panel, the following abbreviations are used:

Ctx		Ctx	
Control (Path) 2 Temporal Ctx	0.0	Control (Path) 4 Parietal Ctx	0.0

Table AC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3294, Run 215669619	Tissue Name	Rel. Exp.(%) Ag3294, Run 215669619
Adipose	0.0	Renal ca. TK-10	0.0
Melanoma* Hs688(A).T	0.0	Bladder	4.9
Melanoma* Hs688(B).T	0.9	Gastric ca. (liver met.) NCI-N87	11.1
Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMV1	0.0	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	1.4	Colon ca. SW480	7.1
Squamous cell carcinoma SCC-4	0.0	Colon ca.* (SW480 met) SW620	1.2
Testis Pool	20.0	Colon ca. HT29	3.2
Prostate ca.* (bone met) PC-3	5.1	Colon ca. HCT-116	2.3
Prostate Pool	3.6	Colon ca. CaCo-2	0.7
Placenta	2.6	Colon cancer tissue	0.0
Uterus Pool	0.0	Colon ca. SW1116	0.5
Ovarian ca. OVCAR-3	17.9	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	1.4	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	0.0	Colon Pool	6.0
Ovarian ca. OVCAR-5	23.7	Small Intestine Pool	2.5
Ovarian ca. IGROV-1	6.2	Stomach Pool	2.6
Ovarian ca. OVCAR-8	1.4	Bone Marrow Pool	0.0
Ovary	1.3	Fetal Heart	0.0
Breast ca. MCF-7	8.0	Heart Pool	2.6
Breast ca. MDA-MB-231	4.1	Lymph Node Pool	3.6
Breast ca. BT 549	4.0	Fetal Skeletal Muscle	1.1
Breast ca. T47D	38.2	Skeletal Muscle Pool	2.0
Breast ca. MDA-N	1.3	Spleen Pool	0.9
Breast Pool	10.5	Thymus Pool	10.2
Trachea	7.2	CNS cancer (glio/astro) U87-MG	0.0
Lung	0.0	CNS cancer (glio/astro) U-118-MG	1.1
Fetal Lung	54.3	CNS cancer (neuro;met) SK-N-AS	100.0
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	2.6	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	0.7	CNS cancer (glio) SNB-19	2.4
Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	33.9
Lung ca. A549	13.3	Brain (Amygdala) Pool	8.4
Lung ca. NCI-H526	2.4	Brain (cerebellum)	23.8
Lung ca. NCI-H23	71.7	Brain (fetal)	5.1
Lung ca. NCI-H460	10.0	Brain (Hippocampus) Pool	26.2
Lung ca. HOP-62	1.4	Cerebral Cortex Pool	13.7
Lung ca. NCI-H522	34.6	Brain (Substantia nigra) Pool	20.7
Liver	3.1	Brain (Thalamus) Pool	26.1
Fetal Liver	2.5	Brain (whole)	15.8
Liver ca. HepG2	0.0	Spinal Cord Pool	15.4
Kidney Pool	6.1	Adrenal Gland	5.6

Fetal Kidney	18.7	Pituitary gland Pool	2.4
Renal ca. 786-0	1.3	Salivary Gland	0.0
Renal ca. A498	7.3	Thyroid (female)	0.0
Renal ca. ACHN	2.9	Pancreatic ca. CAPAN2	5.5
Renal ca. UO-31	0.0	Pancreas Pool	5.3

Table AD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3294, Run 165014460	Tissue Name	Rel. Exp.(%) Ag3294, Run 165014460
Secondary Th1 act	4.5	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	3.1
Secondary Tr1 act	3.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	4.3	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	3.6
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	4.6	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	3.5
CD8 lymphocyte act	0.0	Astrocytes rest	4.5
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	10.2
CD4 lymphocyte none	3.7	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	26.2
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	6.5
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	12.6
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	3.8
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	12.2
Two Way MLR 3 day	12.9	NCI-H292 IFN gamma	3.8
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	6.7	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	2.4
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	7.2
PBMC PHA-L	0.0	Lung fibroblast IL-4	8.9
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	7.6	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0

B lymphocytes CD40L and IL-4	7.3	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	6.3
Monocytes rest	4.2	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	100.0
Macrophages rest	2.1	Lung	43.2
Macrophages LPS	0.0	Thymus	7.6
HUVEC none	2.3	Kidney	3.4
HUVEC starved	3.3		

CNS_neurodegeneration_v1.0 Summary: Ag3294 Results from one experiment with the CG57602-01 gene are not included. The amp plot indicates that there were experimental difficulties with this run.

General_screening_panel_v1.4 Summary: Ag3294 Expression of the CG57602-01 gene is highest in a CNS cancer cell line (CT = 31.8). Therefore, expression of this gene may be used to distinguish this sample from the other samples on this panel. Interestingly, expression of this gene is higher in fetal lung (CT = 32.7) than in adult lung (CT = 40), suggesting that expression of this gene may be used to distinguish adult and fetal lung. Additionally, this gene is expressed at a moderate level in two lung cancer cell lines suggesting a possible role in lung cancer.

In addition, this gene is expressed at low levels in several regions of the central nervous system, including cerebellum, hippocampus, cerebral cortex, substantia nigra, thalamus and spinal cord (CTs = 33.7-35). Therefore, therapeutic modulation of the activity of this gene may be of benefit in the treatment of CNS disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

Panel 4D Summary: Ag3294 Expression of the CG57602-01 gene is highest in colon (CT = 33.3), with low but significant expression also detected in lung (CT = 34.5). Therefore, expression of this gene may be used to distinguish colon and lung from the other tissues on this panel. Furthermore, expression of this gene is decreased in colon samples from patients with IBD colitis and Crohn's disease relative to normal colon. Therefore, therapeutic modulation of the activity of the protein encoded by this gene, using small molecule drugs, antibodies, or protein therapeutics, may be useful in the treatment of inflammatory bowel disease.

NOV2

Expression of NOV2 (CG57558-01) was assessed using the primer-probe set Ag3285, described in Table BA.

Table BA. Probe Name Ag3285

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gacaacaacaagcaaacacaa-3'	22	11	246
Probe	TET-5'-acctccacttcctctggtctgct-3'-TAMRA	26	62	247
Reverse	5'-gcaggagaggaggaagaagag-3'	21	89	248

5 **CNS_neurodegeneration_v1.0 Summary:** Ag3285 Expression of the CG57558-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 1.3D Summary: Ag3285 Expression of the CG57558-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag3285 Expression of the CG57558-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

10 NOV3

Expression of NOV3 (CG57560-01) was assessed using the primer-probe sets Ag3286 and Ag663, described in Tables CA and CB. Results of the RTQ-PCR runs are shown in Tables CC, CD, CE and CF.

Table CA. Probe Name Ag3286

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gaggaggtggaagaagatgatt-3'	22	764	249
Probe	TET-5'-agaatctctccgcaagatcctggct-3'-TAMRA	26	801	250
Reverse	5'-catccaatatggagagtcaaa-3'	22	839	251

15 Table CB. Probe Name Ag663

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-acctttctatgaggaggtggaa-3'	22	754	252
Probe	TET-5'-tgagaaccatgataagaatctctccg-3'-TAMRA	27	787	253
Reverse	5'-gtcaccagccaggatcttg-3'	19	814	254

Table CC. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3286,	Tissue Name	Rel. Exp.(%) Ag3286,
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Ctx		Ctx	
Control 2 Temporal Ctx	70.7	Control 3 Parietal Ctx	11.3
Control 3 Temporal Ctx	14.3	Control (Path) 1 Parietal Ctx	100.0
Control 4 Temporal Ctx	3.5	Control (Path) 2 Parietal Ctx	15.4
Control (Path) 1 Temporal Ctx	87.7	Control (Path) 3 Parietal Ctx	0.7
Control (Path) 2 Temporal Ctx	39.2	Control (Path) 4 Parietal Ctx	33.9

Table CD. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3286, Run 216512997	Tissue Name	Rel. Exp.(%) Ag3286, Run 216512997
Adipose	0.0	Renal ca. TK-10	0.1
Melanoma* Hs688(A).T	0.0	Bladder	0.0
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	0.1
Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	0.0	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.3	Colon ca. SW480	0.6
Squamous cell carcinoma SCC-4	0.0	Colon ca.* (SW480 met) SW620	0.9
Testis Pool	0.2	Colon ca. HT29	0.0
Prostate ca.* (bone met) PC-3	0.0	Colon ca. HCT-116	0.0
Prostate Pool	0.0	Colon ca. CaCo-2	3.1
Placenta	0.0	Colon cancer tissue	0.0

Brain (substantia nigra)	15.6	Lung	0.0
Brain (thalamus)	32.8	Lung (fetal)	0.0
Cerebral Cortex	90.8	Lung ca. (non-s.cell) HOP-62	0.0
Brain (fetal)	100.0	Lung ca. (large cell)NCI-H460	0.0
Brain (whole)	41.8	Lung ca. (non-s.cell) NCI-H23	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (non-sm. cell) A549	0.0
astrocytoma SNB-75	0.0	Lung ca. (s.cell var.) SHP-77	0.0
astrocytoma SW1783	0.0	Lung ca. (small cell) LX-1	0.0
glioma U251	0.0	Lung ca. (small cell) NCI-H69	4.3
glioma SF-295	0.0	Lung ca. (squam.) SW 900	0.0
glioma SNB-19	0.0	Lung ca. (squam.) NCI-H596	16.6
glio/astro U87-MG	0.0	Lymph node	0.0
neuro*; met SK-N-AS	3.8	Spleen	0.0
Mammary gland	0.0	Thymus	0.0
Breast ca. BT-549	0.0	Ovary	0.0
Breast ca. MDA-N	0.0	Ovarian ca. IGROV-1	0.0
Breast ca.* (pl.ef) T47D	0.0	Ovarian ca. OVCAR-3	0.0

Breast ca.* (pl.ef) MCF-7	0.0	Ovarian ca. OVCAR-4	0.0
Breast ca.* (pl.ef) MDA-MB-231	0.0	Ovarian ca. OVCAR-5	0.0
Small intestine	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca.* (ascites) SK-OV-3	0.0
Colon ca. HT29	0.0	Pancreas	0.0
Colon ca. CaCo-2	2.9	Pancreatic ca. CAPAN 2	0.0
Colon ca. HCT-15	0.0	Pituitary gland	5.7
Colon ca. HCT-116	0.0	Placenta	0.0
Colon ca. HCC-2998	0.0	Prostate	0.0
Colon ca. SW480	0.0	Prostate ca.* (bone met) PC-3	0.0
Colon ca.* SW620 (SW480 met)	0.0	Salivary gland	0.0
Stomach	0.0	Trachea	0.0
Gastric ca. (liver met) NCI-N87	0.0	Spinal cord	0.3
Heart	0.0	Testis	0.0
Skeletal muscle (Fetal)	0.0	Thyroid	0.0
Skeletal muscle	0.0	Uterus	0.0
Endothelial cells	0.0	Melanoma M14	0.0
Heart (Fetal)	0.0	Melanoma LOX IMVI	0.0
Kidney	0.0	Melanoma UACC-62	0.0
Kidney (fetal)	0.0	Melanoma SK-MEL-28	0.0
Renal ca. 786-0	0.0	Melanoma* (met)	0.0

		SK-MEL-5	
Renal ca. A498	0.0	Melanoma Hs688(A).T	0.0
Renal ca. ACHN	0.0	Melanoma* (met) Hs688(B).T	0.0
Renal ca. TK-10	0.0		

Table CF. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3286, Run 164633940	Tissue Name	Rel. Exp.(%) Ag3286, Run 164633940
Secondary Th1 act	5.5	HUVEC IL-1beta	0.0
Secondary Th2 act	4.2	HUVEC IFN gamma	0.0
Secondary Tr1 act	15.3	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	33.2	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	24.7	Microvascular Dermal EC none	0.0
Primary Tr1 act	16.2	Microsvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	5.1
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	4.8	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4	0.0	Coronary artery SMC rest	0.0

lymphocyte act			
CD45RO CD4 lymphocyte act	27.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	10.4	Astrocytes rest	3.5
Secondary CD8 lymphocyte rest	18.6	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	7.9	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	17.6
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	7.6	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	26.8	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	4.4	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	11.3	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	14.3	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	2.8

Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	100.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	8.7	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti- CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	6.7
Monocytes LPS	0.0	Colon	49.3
Macrophages rest	1.0	Lung	17.9
Macrophages LPS	6.2	Thymus	0.0
HUVEC none	0.0	Kidney	1.5
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: [Ag3286](#) This panel confirms the expression of this gene at low levels in the brains of an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: [Ag3286](#) The CG57560-01 gene encodes a protein with homology to calmodulin-binding protein kinases. Expression of this gene is highest in the CNS cancer cell line SF-539 (CT = 23.9). Strikingly, this gene is also expressed at moderate to high levels almost exclusively in the CNS; expression is detected amygdala, cerebellum, thalamus, hippocampus, cerebral cortex, substantia nigra and spinal cord. Thus, expression of this gene may be used to distinguish brain from the other samples on this panel.

Furthermore, this brain-specific expression pattern suggests that this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

In addition, moderate expression of this gene is seen in the pituitary gland (CT = 30.6).

5 Therefore, this gene may play a role in endocrine disorders, diabetes, obesity, and growth disorders.

Furthermore, this gene is expressed in most of the lung cancer cell lines on this panel but at undetectable levels in the normal adult lung or fetal tissues. Hence, expression of the CG57560-01 gene might be used as a diagnostic marker for lung cancer. In addition,

10 therapeutic modulation of the activity of this gene, using small molecule drugs, antibodies or protein therapeutics, may be of benefit in the treatment of lung cancer.

Panel 1.1 Summary: Ag663 The CG57560-01 gene is expressed at high levels in all of the CNS samples examined including amygdala, cerebellum, thalamus, hippocampus, cerebral cortex, spinal cord, and the substantia nigra. Highest expression of this gene is seen in the fetal brain sample (CT = 22.1). These results are consistent with what is observed in General_screening_panel_v1.4; please see this panel for a discussion of the relevance of this gene in the central nervous system.

Panel 4D Summary: Ag3286 Expression of the CG57560-01 gene is highest in pokeweed mitogen stimulated peripheral blood mononuclear cells (CT = 32.7) Expression of this transcript in B cells suggests that this gene may be involved in rheumatic disease including rheumatoid arthritis, lupus, osteoarthritis, and hyperproliferative B cell disorders.

In addition, low but significant expression of this gene is seen in activated T cells and memory T cells, but not resting T cells, suggesting that CG57560-01 gene expression may play a role in T cell mediated diseases such as autoimmunity or delayed type hypersensitivity reactions.

NOV4

Expression of NOV4a (CG57547-01) and NOV4b CG57547-02 was assessed using the primer-probe sets Ag3690, Ag531, Ag534 and Ag535, described in Tables DA, DB, DC and DD. Results of the RTQ-PCR runs are shown in Tables DE, DF, DG, DH, DI, DJ and DK. Please note that the CG57547-02 variant is not recognized by primer-probe set Ag3690.

Table DA. Probe Name Ag3690

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-agacgtcaaacagggaatctt-3'	22	1744	255
Probe	TET-5'-cctccaggatataagatcactctgattga-3'-TAMRA	29	1766	256

Reverse	5'-tctgttaggttctcccatgag-3'	21	1817	257
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Table DB. Probe Name Ag531

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-tccaggatataagatcactctgattgata-3'	29	1768	258
Probe	TET-5'-agggttctcccatgagataattcaataacaagtcct-3'-TAMRA	35	1798	259
Reverse	5'-aacgttctctagtaggtgcattgc-3'	26	1834	260

Table DC. Probe Name Ag534

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-tcagtatacaattgccataatttctt-3'	28	3039	261
Probe	TET-5'-tttgctcaaatcttagtccaaatccaatgaa-3'-TAMRA	32	3068	262
Reverse	5'-aaaacatgattatcatatgcatttgc-3'	27	3110	263

Table DD. Probe Name Ag535

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-tttacaagtgaaggcaatttccaa-3'	24	3562	264
Probe	TET-5'-agccataataaaatgataacgctgggtacttccatacat-3'-TAMRA	39	3587	265
Reverse	5'-gaggcagaactggtttctcatga-3'	23	3628	266

Table DE. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3690, Run 211144703	Tissue Name	Rel. Exp.(%) Ag3690, Run 211144703
AD 1 Hippo	17.9	Control (Path) 3 Temporal Ctx	4.3
AD 2 Hippo	20.0	Control (Path) 4 Temporal Ctx	39.5
AD 3 Hippo	17.2	AD 1 Occipital Ctx	38.2
AD 4 Hippo	6.1	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	97.3	AD 3 Occipital Ctx	11.8
AD 6 Hippo	62.4	AD 4 Occipital Ctx	28.5
Control 2 Hippo	23.2	AD 5 Occipital Ctx	25.0
Control 4 Hippo	12.4	AD 6 Occipital Ctx	45.4
Control (Path) 3 Hippo	22.4	Control 1 Occipital Ctx	5.1
AD 1 Temporal Ctx	34.2	Control 2 Occipital Ctx	51.1
AD 2 Temporal Ctx	37.1	Control 3 Occipital Ctx	24.8
AD 3 Temporal Ctx	12.2	Control 4 Occipital Ctx	11.7
AD 4 Temporal Ctx	27.0	Control (Path) 1 Occipital Ctx	100.0
AD 5 Inf Temporal Ctx	85.3	Control (Path) 2 Occipital Ctx	22.5
AD 5 SupTemporal Ctx	87.7	Control (Path) 3 Occipital Ctx	2.8
AD 6 Inf Temporal Ctx	80.7	Control (Path) 4 Occipital Ctx	29.7
AD 6 Sup Temporal Ctx	82.9	Control 1 Parietal Ctx	14.0
Control 1 Temporal Ctx	7.9	Control 2 Parietal Ctx	62.4
Control 2 Temporal Ctx	23.7	Control 3 Parietal Ctx	18.3
Control 3 Temporal Ctx	19.3	Control (Path) 1 Parietal Ctx	74.7
Control 4 Temporal Ctx	9.1	Control (Path) 2 Parietal Ctx	33.4
Control (Path) 1 Temporal Ctx	56.6	Control (Path) 3 Parietal Ctx	5.1
Control (Path) 2 Temporal Ctx	43.2	Control (Path) 4 Parietal Ctx	48.6

Tissue Name	Rel. Exp.(%) Ag3690, Run 217130999	Tissue Name	Rel. Exp.(%) Ag3690, Run 217130999
Adipose	12.6	Renal ca. TK-10	26.8
Melanoma* Hs688(A).T	32.5	Bladder	24.1
Melanoma* Hs688(B).T	31.0	Gastric ca. (liver met.) NCI-N87	61.1
Melanoma* M14	53.6	Gastric ca. KATO III	38.2
Melanoma* LOXIMVI	20.0	Colon ca. SW-948	6.1
Melanoma* SK-MEL-5	57.0	Colon ca. SW480	22.5
Squamous cell carcinoma SCC-4	11.6	Colon ca.* (SW480 met) SW620	35.4
Testis Pool	10.1	Colon ca. HT29	20.7
Prostate ca.* (bone met) PC-3	39.2	Colon ca. HCT-116	37.1
Prostate Pool	11.3	Colon ca. CaCo-2	66.0
Placenta	3.8	Colon cancer tissue	16.7
Uterus Pool	8.1	Colon ca. SW1116	5.1
Ovarian ca. OVCAR-3	26.1	Colon ca. Colo-205	8.0
Ovarian ca. SK-OV-3	34.9	Colon ca. SW-48	3.7
Ovarian ca. OVCAR-4	3.7	Colon Pool	22.4
Ovarian ca. OVCAR-5	40.1	Small Intestine Pool	20.4
Ovarian ca. IGROV-1	11.7	Stomach Pool	11.0
Ovarian ca. OVCAR-8	15.1	Bone Marrow Pool	9.2
Ovary	15.6	Fetal Heart	27.0
Breast ca. MCF-7	100.0	Heart Pool	13.3
Breast ca. MDA-MB-231	20.9	Lymph Node Pool	27.5
Breast ca. BT 549	52.1	Fetal Skeletal Muscle	5.6
Breast ca. T47D	54.0	Skeletal Muscle Pool	15.8
Breast ca. MDA-N	16.7	Spleen Pool	15.9
Breast Pool	24.3	Thymus Pool	24.5
Trachea	10.6	CNS cancer (glio/astro) U87-MG	63.3
Lung	6.7	CNS cancer (glio/astro) U-118-MG	54.7
Fetal Lung	32.3	CNS cancer (neuro;met) SK-N-AS	24.1
Lung ca. NCI-N417	5.6	CNS cancer (astro) SF-539	27.0
Lung ca. LX-1	34.6	CNS cancer (astro) SNB-75	55.1
Lung ca. NCI-H146	2.9	CNS cancer (glio) SNB-19	14.9
Lung ca. SHP-77	19.8	CNS cancer (glio) SF-295	66.4
Lung ca. A549	35.8	Brain (Amygdala) Pool	4.6
Lung ca. NCI-H526	4.7	Brain (cerebellum)	7.9
Lung ca. NCI-H23	47.3	Brain (fetal)	14.0
Lung ca. NCI-H460	27.9	Brain (Hippocampus) Pool	6.4
Lung ca. HOP-62	10.1	Cerebral Cortex Pool	7.4
Lung ca. NCI-H522	24.0	Brain (Substantia nigra) Pool	5.0
Liver	1.4	Brain (Thalamus) Pool	10.7
Fetal Liver	25.2	Brain (whole)	6.5
Liver ca. HepG2	12.1	Spinal Cord Pool	8.0
Kidney Pool	29.9	Adrenal Gland	7.2
Fetal Kidney	31.2	Pituitary gland Pool	4.5
Renal ca. 786-0	26.1	Salivary Gland	2.3
Renal ca. A498	15.4	Thyroid (female)	5.2

Renal ca. ACHN	14.3	Pancreatic ca. CAPAN2	15.3
Renal ca. UO-31	12.2	Pancreas Pool	27.4

Table DG. Panel 1.1

Tissue Name	Rel. Exp.(%) Ag534, Run 111162676	Tissue Name	Rel. Exp.(%) Ag534, Run 111162676
Adrenal gland	21.2	Renal ca. UO-31	6.3
Bladder	57.8	Renal ca. RXF 393	4.4
Brain (amygdala)	3.7	Liver	59.5
Brain (cerebellum)	59.9	Liver (fetal)	13.8
Brain (hippocampus)	15.0	Liver ca. (hepatoblast) HepG2	13.7
Brain (substantia nigra)	21.5	Lung	5.6
Brain (thalamus)	7.6	Lung (fetal)	6.6
Cerebral Cortex	12.9	Lung ca. (non-s.cell) HOP-62	50.3
Brain (fetal)	17.9	Lung ca. (large cell)NCI-H460	47.6
Brain (whole)	9.9	Lung ca. (non-s.cell) NCI-H23	27.7
glio/astro U-118-MG	12.3	Lung ca. (non-s.cl) NCI-H522	74.2
astrocytoma SF-539	27.0	Lung ca. (non-sm. cell) A549	32.1
astrocytoma SNB-75	7.6	Lung ca. (s.cell var.) SHP-77	7.6
astrocytoma SW1783	4.9	Lung ca. (small cell) LX-1	52.5
glioma U251	18.0	Lung ca. (small cell) NCI-H69	39.2
glioma SF-295	31.2	Lung ca. (squam.) SW 900	12.6
glioma SNB-19	35.6	Lung ca. (squam.) NCI-H596	34.6
glio/astro U87-MG	35.4	Lymph node	10.4
neuro*; met SK-N-AS	32.5	Spleen	6.4
Mammary gland	10.7	Thymus	13.1
Breast ca. BT-549	8.0	Ovary	2.9
Breast ca. MDA-N	32.1	Ovarian ca. IGROV-1	21.9
Breast ca. * (pl.ef) T47D	62.9	Ovarian ca. OVCAR-3	11.7
Breast ca. * (pl.ef) MCF-7	98.6	Ovarian ca. OVCAR-4	4.5
Breast ca. * (pl.ef) MDA-MB-231	7.4	Ovarian ca. OVCAR-5	42.3
Small intestine	24.8	Ovarian ca. OVCAR-8	51.4
Colorectal	3.1	Ovarian ca. * (ascites) SK-OV-3	28.1
Colon ca. HT29	24.7	Pancreas	39.5
Colon ca. CaCo-2	48.0	Pancreatic ca. CAPAN 2	4.3
Colon ca. HCT-15	15.3	Pituitary gland	28.7
Colon ca. HCT-116	21.3	Placenta	27.5
Colon ca. HCC-2998	53.2	Prostate	23.0
Colon ca. SW480	5.2	Prostate ca. * (bone met) PC-3	32.1
Colon ca. * SW620 (SW480 met)	44.4	Salivary gland	41.2
Stomach	13.0	Trachea	15.3
Gastric ca. (liver met) NCI-N87	67.4	Spinal cord	14.1
Heart	44.1	Testis	9.8

Skeletal muscle (Fetal)	6.1	Thyroid	19.2
Skeletal muscle	54.0	Uterus	17.1
Endothelial cells	17.2	Melanoma M14	26.6
Heart (Fetal)	6.5	Melanoma LOX IMV1	5.3
Kidney	100.0	Melanoma UACC-62	15.5
Kidney (fetal)	30.4	Melanoma SK-MEL-28	80.7
Renal ca. 786-0	15.9	Melanoma* (met) SK-MEL-5	39.5
Renal ca. A498	16.4	Melanoma Hs688(A).T	14.9
Renal ca. ACHN	11.3	Melanoma* (met) Hs688(B).T	16.3
Renal ca. TK-10	25.9		

Table DH, Panel 1.2

Tissue Name	Rel. Exp.(%) Ag535, Run 112162329	Tissue Name	Rel. Exp.(%) Ag535, Run 112162329
Endothelial cells	10.2	Renal ca. 786-0	14.6
Heart (Fetal)	1.5	Renal ca. A498	21.8
Pancreas	94.0	Renal ca. RXF 393	5.5
Pancreatic ca. CAPAN 2	8.4	Renal ca. ACHN	13.4
Adrenal Gland	41.5	Renal ca. UO-31	5.8
Thyroid	29.1	Renal ca. TK-10	22.2
Salivary gland	47.0	Liver	56.3
Pituitary gland	48.3	Liver (fetal)	20.6
Brain (fetal)	17.1	Liver ca. (hepatoblast) HepG2	11.3
Brain (whole)	41.8	Lung	14.0
Brain (amygdala)	9.3	Lung (fetal)	20.7
Brain (cerebellum)	20.0	Lung ca. (small cell) LX-1	48.3
Brain (hippocampus)	20.7	Lung ca. (small cell) NCI-H69	27.4
Brain (thalamus)	17.6	Lung ca. (s.cell var.) SHP-77	5.6
Cerebral Cortex	11.9	Lung ca. (large cell) NCI-H460	61.1
Spinal cord	12.0	Lung ca. (non-sm. cell) A549	25.9
glio/astro U87-MG	45.1	Lung ca. (non-s.cell) NCI-H23	22.4
glio/astro U-118-MG	20.0	Lung ca. (non-s.cell) HOP-62	34.9
astrocytoma SW1783	6.3	Lung ca. (non-s.cl) NCI-H522	100.0
neuro*; met SK-N-AS	34.4	Lung ca. (squam.) SW 900	15.8
astrocytoma SF-539	22.2	Lung ca. (squam.) NCI-H596	40.3
astrocytoma SNB-75	9.6	Mammary gland	30.4
glioma SNB-19	31.0	Breast ca.* (pl.ef) MCF-7	70.7
glioma U251	24.7	Breast ca.* (pl.ef) MDA-MB-231	6.6
glioma SF-295	27.7	Breast ca.* (pl. ef) T47D	37.9
Heart	49.3	Breast ca. BT-549	16.6
Skeletal Muscle	48.6	Breast ca. MDA-N	31.4
Bone marrow	23.2	Ovary	2.5
Thymus	17.7	Ovarian ca. OVCAR-3	25.5
Spleen	22.5	Ovarian ca. OVCAR-4	5.6

Lymph node	33.0	Ovarian ca. OVCAR-5	45.1
Colorectal Tissue	1.5	Ovarian ca. OVCAR-8	23.3
Stomach	24.7	Ovarian ca. IGROV-1	27.2
Small intestine	34.4	Ovarian ca. (ascites) SK-OV-3	33.9
Colon ca. SW480	5.0	Uterus	21.2
Colon ca. * SW620 (SW480 met)	25.3	Placenta	60.7
Colon ca. HT29	20.3	Prostate	25.3
Colon ca. HCT-116	20.4	Prostate ca. * (bone met) PC-3	59.9
Colon ca. CaCo-2	39.8	Testis	37.1
Colon ca. Tissue (ODO3866)	2.5	Melanoma Hs688(A).T	14.5
Colon ca. HCC-2998	54.7	Melanoma* (met) Hs688(B).T	18.7
Gastric ca.* (liver met) NCI-N87	69.3	Melanoma UACC-62	19.1
Bladder	43.8	Melanoma M14	25.2
Trachea	13.2	Melanoma LOX IMVI	4.2
Kidney	48.3	Melanoma* (met) SK-MEL-5	50.0
Kidney (fetal)	51.8		

Table DJ. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag531, Run 165974812	Tissue Name	Rel. Exp.(%) Ag531, Run 165974812
Liver adenocarcinoma	22.1	Kidney (fetal)	17.0
Pancreas	6.8	Renal ca. 786-0	15.7
Pancreatic ca. CAPAN 2	19.3	Renal ca. A498	22.4
Adrenal gland	3.8	Renal ca. RXF 393	30.8
Thyroid	3.8	Renal ca. ACHN	10.7
Salivary gland	10.4	Renal ca. UO-31	10.7
Pituitary gland	15.8	Renal ca. TK-10	12.3
Brain (fetal)	11.8	Liver	10.9
Brain (whole)	30.6	Liver (fetal)	10.0
Brain (amygdala)	16.8	Liver ca. (hepatoblast) HepG2	20.2
Brain (cerebellum)	45.4	Lung	8.5
Brain (hippocampus)	20.3	Lung (fetal)	18.7
Brain (substantia nigra)	7.6	Lung ca. (small cell) LX-1	49.0
Brain (thalamus)	21.9	Lung ca. (small cell) NCI-H69	50.3
Cerebral Cortex	9.0	Lung ca. (s.cell var.) SHP-77	23.5
Spinal cord	27.5	Lung ca. (large cell) NCI-H460	11.7
glio/astro U87-MG	40.1	Lung ca. (non-sm. cell) A549	10.2
glio/astro U-118-MG	26.4	Lung ca. (non-s.cell) NCI-H23	30.4
astrocytoma SW1783	21.3	Lung ca. (non-s.cell) HOP-62	13.5
neuro*; met SK-N-AS	13.0	Lung ca. (non-s.cl) NCI-H522	12.9
astrocytoma SF-539	68.3	Lung ca. (squam.) SW 900	22.5
astrocytoma SNB-75	12.3	Lung ca. (squam.) NCI-	49.0

		H596	
glioma SNB-19	65.1	Mammary gland	5.9
glioma U251	29.9	Breast ca.* (pl.ef) MCF-7	100.0
glioma SF-295	11.8	Breast ca.* (pl.ef) MDA-MB-231	7.7
Heart (fetal)	3.0	Breast ca.* (pl.ef) T47D	18.9
Heart	9.7	Breast ca. BT-549	14.2
Skeletal muscle (fetal)	1.2	Breast ca. MDA-N	8.6
Skeletal muscle	11.0	Ovary	1.5
Bone marrow	19.5	Ovarian ca. OVCAR-3	11.3
Thymus	16.2	Ovarian ca. OVCAR-4	7.5
Spleen	11.3	Ovarian ca. OVCAR-5	34.6
Lymph node	25.0	Ovarian ca. OVCAR-8	20.9
Colorectal	10.5	Ovarian ca. IGROV-1	11.0
Stomach	11.1	Ovarian ca.* (ascites) SK-OV-3	41.5
Small intestine	17.1	Uterus	9.9
Colon ca. SW480	8.7	Placenta	26.4
Colon ca.* SW620(SW480 met)	24.8	Prostate	5.7
Colon ca. HT29	14.3	Prostate ca.* (bone met)PC-3	31.0
Colon ca. HCT-116	13.0	Testis	9.0
Colon ca. CaCo-2	50.7	Melanoma Hs688(A).T	11.7
Colon ca. tissue(ODO3866)	18.7	Melanoma* (met) Hs688(B).T	21.9
Colon ca. HCC-2998	36.1	Melanoma UACC-62	20.4
Gastric ca.* (liver met) NCI-N87	48.6	Melanoma M14	31.4
Bladder	22.4	Melanoma LOX IMVI	3.7
Trachea	3.1	Melanoma* (met) SK-MEL-5	19.5
Kidney	13.0	Adipose	11.0

Table DJ. Panel 4.1D

Tissue Name	Rel. Exp.(%) Ag3690, Run 169988048	Tissue Name	Rel. Exp.(%) Ag3690, Run 169988048
Secondary Th1 act	69.7	HUVEC IL-1beta	22.7
Secondary Th2 act	77.4	HUVEC IFN gamma	33.9
Secondary Tr1 act	79.6	HUVEC TNF alpha + IFN gamma	25.5
Secondary Th1 rest	28.7	HUVEC TNF alpha + IL4	29.3
Secondary Th2 rest	39.2	HUVEC IL-11	14.8
Secondary Tr1 rest	38.7	Lung Microvascular EC none	45.4
Primary Th1 act	64.2	Lung Microvascular EC TNFalpha + IL-1beta	43.8
Primary Th2 act	79.6	Microvascular Dermal EC none	35.4
Primary Tr1 act	76.3	Microvascular Dermal EC TNFalpha + IL-1beta	34.6
Primary Th1 rest	45.1	Bronchial epithelium TNFalpha + IL1beta	57.4
Primary Th2 rest	38.2	Small airway epithelium none	12.4
Primary Tr1 rest	64.6	Small airway epithelium TNFalpha + IL-1beta	23.2
CD45RA CD4 lymphocyte act	52.9	Coronary artery SMC rest	26.8
CD45RO CD4 lymphocyte	84.1	Coronary artery SMC TNFalpha +	20.3

act		IL-1beta	
CD8 lymphocyte act	75.8	Astrocytes rest	20.4
Secondary CD8 lymphocyte rest	74.2	Astrocytes TNFalpha + IL-1beta	22.1
Secondary CD8 lymphocyte act	33.0	KU-812 (Basophil) rest	45.1
CD4 lymphocyte none	26.6	KU-812 (Basophil) PMA/ionomycin	85.9
2ry Th1/Th2/Tr1_anti-CD95 CH11	49.7	CCD1106 (Keratinocytes) none	39.8
LAK cells rest	57.8	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	33.0
LAK cells IL-2	66.0	Liver cirrhosis	18.2
LAK cells IL-2+IL-12	51.8	NCI-H292 none	31.9
LAK cells IL-2+IFN gamma	68.3	NCI-H292 IL-4	38.2
LAK cells IL-2+ IL-18	68.3	NCI-H292 IL-9	64.6
LAK cells PMA/ionomycin	56.6	NCI-H292 IL-13	37.9
NK Cells IL-2 rest	66.4	NCI-H292 IFN gamma	50.0
Two Way MLR 3 day	80.1	HPAEC none	27.7
Two Way MLR 5 day	59.5	HPAEC TNF alpha + IL-1 beta	49.0
Two Way MLR 7 day	44.1	Lung fibroblast none	50.7
PBMC rest	22.5	Lung fibroblast TNF alpha + IL-1 beta	18.3
PBMC PWM	74.7	Lung fibroblast IL-4	38.7
PBMC PHA-L	59.9	Lung fibroblast IL-9	52.5
Ramos (B cell) none	100.0	Lung fibroblast IL-13	37.9
Ramos (B cell) ionomycin	88.9	Lung fibroblast IFN gamma	41.8
B lymphocytes PWM	50.0	Dermal fibroblast CCD1070 rest	52.9
B lymphocytes CD40L and IL-4	88.9	Dermal fibroblast CCD1070 TNF alpha	84.7
EOL-1 dbcAMP	54.3	Dermal fibroblast CCD1070 IL-1 beta	27.7
EOL-1 dbcAMP PMA/ionomycin	73.2	Dermal fibroblast IFN gamma	30.1
Dendritic cells none	59.9	Dermal fibroblast IL-4	80.1
Dendritic cells LPS	53.2	Dermal Fibroblasts rest	37.6
Dendritic cells anti-CD40	61.1	Neutrophils TNFa+LPS	28.9
Monocytes rest	59.9	Neutrophils rest	13.9
Monocytes LPS	55.5	Colon	21.6
Macrophages rest	49.0	Lung	30.1
Macrophages LPS	28.9	Thymus	92.0
HUVEC none	16.2	Kidney	74.7
HUVEC starved	27.9		

Table DK. Panel 4D

Tissue Name	Rel. Exp.(%) Ag531, Run 165919167	Tissue Name	Rel. Exp.(%) Ag531, Run 165919167
Secondary Th1 act	18.4	HUVEC IL-1beta	2.1
Secondary Th2 act	0.0	HUVEC IFN gamma	5.4
Secondary Tr1 act	16.8	HUVEC TNF alpha + IFN gamma	6.1
Secondary Th1 rest	4.4	HUVEC TNF alpha + IL4	6.6
Secondary Th2 rest	7.8	HUVEC IL-11	3.4
Secondary Tr1 rest	7.3	Lung Microvascular EC none	5.8
Primary Th1 act	5.1	Lung Microvascular EC TNFalpha + IL-1beta	7.0
Primary Th2 act	16.6	Microvascular Dermal EC none	7.2

Primary Tr1 act	18.3	Microvascular Dermal EC TNFalpha + IL-1beta	5.8
Primary Th1 rest	31.9	Bronchial epithelium TNFalpha + IL1beta	8.4
Primary Th2 rest	16.2	Small airway epithelium none	2.2
Primary Tr1 rest	8.4	Small airway epithelium TNFalpha + IL-1beta	14.4
CD45RA CD4 lymphocyte act	10.2	Coronary artery SMC rest	3.9
CD45RO CD4 lymphocyte act	17.4	Coronary artery SMC TNFalpha + IL-1beta	3.9
CD8 lymphocyte act	13.7	Astrocytes rest	3.7
Secondary CD8 lymphocyte rest	15.6	Astrocytes TNFalpha + IL-1beta	3.3
Secondary CD8 lymphocyte act	10.5	KU-812 (Basophil) rest	10.3
CD4 lymphocyte none	4.2	KU-812 (Basophil) PMA/ionomycin	31.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	10.3	CCD1106 (Keratinocytes) none	7.3
LAK cells rest	15.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	1.8
LAK cells IL-2	14.9	Liver cirrhosis	2.2
LAK cells IL-2+IL-12	10.1	Lupus kidney	1.8
LAK cells IL-2+IFN gamma	15.7	NCI-H292 none	12.5
LAK cells IL-2+ IL-18	14.8	NCI-H292 IL-4	17.1
LAK cells PMA/ionomycin	11.7	NCI-H292 IL-9	8.5
NK Cells IL-2 rest	13.2	NCI-H292 IL-13	15.5
Two Way MLR 3 day	18.3	NCI-H292 IFN gamma	12.9
Two Way MLR 5 day	8.0	HPAEC none	5.7
Two Way MLR 7 day	7.1	HPAEC TNF alpha + IL-1 beta	7.3
PBMC rest	4.9	Lung fibroblast none	8.4
PBMC PWM	61.6	Lung fibroblast TNF alpha + IL-1 beta	4.0
PBMC PHA-L	19.8	Lung fibroblast IL-4	13.6
Ramos (B cell) none	19.1	Lung fibroblast IL-9	9.7
Ramos (B cell) ionomycin	100.0	Lung fibroblast IL-13	7.9
B lymphocytes PWM	36.1	Lung fibroblast IFN gamma	11.7
B lymphocytes CD40L and IL-4	25.0	Dermal fibroblast CCD1070 rest	14.4
EOL-1 dbcAMP	13.0	Dermal fibroblast CCD1070 TNF alpha	50.0
EOL-1 dbcAMP PMA/ionomycin	13.4	Dermal fibroblast CCD1070 IL-1 beta	10.8
Dendritic cells none	7.0	Dermal fibroblast IFN gamma	10.1
Dendritic cells LPS	8.3	Dermal fibroblast IL-4	22.1
Dendritic cells anti-CD40	8.7	IBD Colitis 2	1.4
Monocytes rest	7.3	IBD Crohn's	1.5
Monocytes LPS	6.7	Colon	11.8
Macrophages rest	9.6	Lung	6.8
Macrophages LPS	4.2	Thymus	33.0
HUVEC none	3.9	Kidney	22.7
HUVEC starved	8.0		

CNS_neurodegeneration_v1.0 Summary: Ag3690 This panel confirms the expression of the CG57547-01 gene at low levels in the brain in an independent group of

individuals. Interestingly, this gene appears to be upregulated in the temporal cortex of Alzheimer's disease patients. Therefore, blockade of the transient receptor potential-related protein encoded for by this gene may be of use in the treatment of this disease and decrease neuronal death. Ag531 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown). It is likely that there were experimental difficulties with this run.

General_screening_panel_v1.4 Summary: Ag3690 The CG57547-01 gene is expressed at moderate levels across all of the samples on this panel with highest expression detected in breast cancer cell line MCF-7 (CT = 27.5). In general, the pattern of gene expression is consistent with that observed in Panels 1.1 and 1.2. Please see Panel 1.1 for a discussion of the potential relevance of this expression pattern in CNS and metabolically relevant tissues.

In addition, consistent with what is seen in Panel 1.2, this gene is expressed at higher levels in fetal liver (CT = 29.5) than in adult liver (CT = 33.6). Therefore, expression of this gene may be used to distinguish fetal liver from adult liver.

Panel 1.1 Summary: Ag534 The CG57547-01 gene encodes a protein with homology to melastatin, a member of the transient receptor potential (Trp) family of calcium ion channels. The CG57547-01 gene is expressed at moderate to high levels across all the samples on this panel with the highest expression detected in kidney (CT = 25). Interestingly, defects in ion channels are associated with kidney disorders, such as Bartter's syndrome, polycystic kidney disease and Dent's disease (ref. 1), suggesting that the CG57547-01 gene may also play a role in kidney homeostasis.

Furthermore, this gene is expressed in a variety of metabolically relevant tissues, including adrenal gland, heart, skeletal muscle, liver, pancreas, pituitary gland, and thyroid. Therefore, as a classical drug target, the CG57547-01 protein may be useful for the treatment of disease in any or all of these tissues, including diabetes and obesity. In support of this hypothesis, mutations in ion channels have previously been associated with hyperinsulinemic hypoglycemia of infancy (ref. 1).

Among CNS samples, the CG57547-01 gene is expressed in hippocampus, substantia nigra, thalamus, and cerebral cortex with highest expression detected in the cerebellum (CT values < 30). The protein encoded by the CG57547-01 gene shows considerable homology to known ion channels, which are the primary targets of all known antiepileptics. Furthermore, all gene mutations known to cause epilepsy or seizure disorders are found in ion channels (ref.

1-2). Two established antiepileptics (valproate and carbamazepine) also have efficacy in the treatment of bipolar disorder. Therefore, therapeutic modulation of this gene or its protein product may be beneficial in the treatment of these disorders as may agonism/antagonism of the ion channel.

Interestingly, it also appears that there is a difference in CG57547-01 gene expression between several adult tissues and their fetal counterparts. Specifically, expression of this gene is significantly higher in adult kidney, liver, skeletal muscle and heart when compared to the corresponding fetal tissues. Thus, the expression of the CG57547-01 gene could be used as a marker of adult tissues, or alternatively its relative absence could be used as a marker of fetal tissues. Since fetal tissues show potential use for organ regeneration, the expression of this gene may be inhibitory to organogenesis. Thus, the therapeutic modulation of the activity of the CG57547-01 gene product, through the use of small molecule drugs or antibodies, might be of use for the treatment of diseases whose pathology is characterized by organ degeneration.

References:

1. Dworakowska B., Dolowy K. (2000) Ion channels-related diseases. *Acta Biochim. Pol.* 47: 685-703.

There are many diseases related to ion channels. Mutations in muscle voltage-gated sodium, potassium, calcium and chloride channels, and acetylcholine-gated channel may lead to such physiological disorders as hyper- and hypokalemic periodic paralysis, myotonias, long QT syndrome, Brugada syndrome, malignant hyperthermia and myasthenia. Neuronal disorders, e.g., epilepsy, episodic ataxia, familial hemiplegic migraine, Lambert-Eaton myasthenic syndrome, Alzheimer's disease, Parkinson's disease, schizophrenia, hyperekplexia may result from dysfunction of voltage-gated sodium, potassium and calcium channels, or acetylcholine- and glycine-gated channels. Some kidney disorders, e.g., Bartter's syndrome, polycystic kidney disease and Dent's disease, secretion disorders, e.g., hyperinsulinemic hypoglycemia of infancy and cystic fibrosis, vision disorders, e.g., congenital stationary night blindness and total colour-blindness may also be linked to mutations in ion channels.

PMID: 11310970

2. Li M., Lester H.A. (2001) Ion channel diseases of the central nervous system. *CNS Drug Rev.* 7: 214-240.

In the last decade, advances in molecular genetics and cellular electrophysiology have increased our understanding of ion channel function. A number of diseases termed

"channelopathies" have been discovered that are caused by ion channel dysfunction. Channelopathies can be caused by autoimmune, iatrogenic, toxic or genetic mechanisms. Mutations in genes encoding ion channel proteins that disrupt channel function are now the most commonly identified cause of channelopathies, perhaps because gene disruption is readily detected by the methods of molecular genetics. Ion channels are abundant in the central nervous system (CNS), but CNS channelopathies are rare; however, they overlap with some important neurological disorders, such as epilepsy, ataxia, migraine, schizophrenia, Alzheimer's disease and other neurodegenerative diseases. It is possible that more CNS channelopathies will be discovered when additional ion channels are characterized and the complex mechanisms of brain function are better understood. At present, increased knowledge of the identity, structure and function of ion channels is facilitating diagnosis and treatment of many channelopathies.

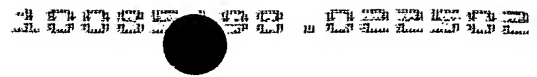
PMID: 11474425

Panel 1.2 Summary: Ag535 The CG57547-01 gene is expressed at moderate to high levels across all the samples on this panel with the highest expression detected in lung cancer cell line NCI-H522 (CT = 25). In general, the pattern of CG57547-01 gene expression is consistent with that observed in Panel 1.1; see Panel 1.1 for discussion of expression pattern in CNS and metabolically relevant tissues.

Interestingly, there appears to be a difference in CG57547-01 gene expression between fetal and adult liver. In addition, this gene is also highly expressed in pancreas (CT = 25). Thus, the relative expression of the CG57547-01 gene might be useful as a marker of pancreas tissue. Furthermore, since this gene appears to be differentially expressed in adult and fetal liver, and that fetal liver represents a state of organogenesis, the therapeutic down-modulation of this gene product, through the use of small molecule drugs or antibodies might be of use in the treatment of diseases involving liver degeneration.

Panel 1.3D Summary: Ag531 This probe/primer set produced a similar pattern of expression as is seen in Panels 1.1, 1.2, and 1.4 using different probe/primer sets, although the expression level is lower in this experiment. This gene is expressed at highest levels in the breast cancer cell line MCF-7 (CT = 33) and is also expressed at low levels in a number of other samples on this panel. Please see Panel 1.1 for discussion of expression pattern in CNS and metabolically relevant tissues.

Panel 4.1D Summary: Ag3690 The CG57547-01 gene is expressed at low to moderate levels in each of the cells and tissues examined on this panel. This observation



suggests that this gene plays an important role in a variety of immunologically relevant cell types. Interestingly, calcium release activated calcium channels have been shown to be required for T cell activation, cytokine synthesis, and proliferation (ref. 1).

References:

1. Lepple-Wienhues A., Belka C., Laun T., Jekle A., Walter B., Wieland U., Welz M., Heil L., Kun J., Busch G., Weller M., Bamberg M., Gulbins E., Lang F. (1999) Stimulation of CD95 (Fas) blocks T lymphocyte calcium channels through sphingomyelinase and sphingolipids. *Proc. Natl. Acad. Sci. U S A* 96: 13795-13800.

Calcium influx through store-operated calcium release-activated calcium channels (CRAC) is required for T cell activation, cytokine synthesis, and proliferation. The CD95 (Apo-1/Fas) receptor plays a role in self-tolerance and tumor immune escape, and it mediates apoptosis in activated T cells. CD95-stimulation blocks CRAC and Ca(2+) influx in lymphocytes through the activation of acidic sphingomyelinase (ASM) and ceramide release. The block of Ca(2+) entry is lacking in CD95-defective lpr lymphocytes as well as in ASM-defective cells and can be restored by retransfection of ASM. C2 ceramide, C6 ceramide, and sphingosine block CRAC reversibly, whereas the inactive dihydroceramide has no effect. CD95-stimulation or the addition of ceramide prevents store-operated Ca(2+) influx, activation of the transcriptional regulator NFAT, and IL-2 synthesis. The block of CRAC by sphingomyelinase metabolites adds a function to the repertoire of the CD95 receptor inhibiting T cell activation signals.

PMID: 10570152

Panel 4D Summary: Ag531 This probe/primer set produced a similar pattern of expression as was seen in Panel 4.1D using probe/primer set Ag3690, although the levels of expression are lower on Panel 4D. Expression of the CG57547-01 gene is highest in Ramos B cells treated with ionomycin (CT = 30.4). Moderate expression of this gene is also seen in other B cell samples including peripheral blood mononuclear cells treated with pokeweed mitogen and B lymphocytes. Expression of this transcript in B cells suggests that this gene may be involved in rheumatic disease including rheumatoid arthritis, lupus, osteoarthritis, and hyperproliferative B cell disorders. Low but significant expression of this gene is seen in the other samples on this panel.

NOV6

Expression of gene NOV6/CG57611-01 was assessed using the primer-probe set Ag3295, described in Table EA. Results of the RTQ-PCR runs are shown in Tables EB, EC and ED.

Table EA. Probe Name Ag3295

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-caagccttcctcactgttaag-3'	22	396	267
Probe	TET-5'-ccccagcttcaaacatttctactcaa-3'-TAMRA	26	419	268
Reverse	5'-gcctcaacagacagtttggtat-3'	22	452	269

5 Table EB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3295, Run 210062303	Tissue Name	Rel. Exp.(%) Ag3295, Run 210062303
AD 1 Hippo	9.7	Control (Path) 3 Temporal Ctx	17.0
AD 2 Hippo	29.1	Control (Path) 4 Temporal Ctx	40.6
AD 3 Hippo	28.3	AD 1 Occipital Ctx	32.8
AD 4 Hippo	8.1	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	17.4	AD 3 Occipital Ctx	29.3
AD 6 Hippo	64.6	AD 4 Occipital Ctx	15.0
Control 2 Hippo	63.7	AD 5 Occipital Ctx	66.0
Control 4 Hippo	16.6	AD 6 Occipital Ctx	73.2
Control (Path) 3 Hippo	0.0	Control 1 Occipital Ctx	8.5
AD 1 Temporal Ctx	41.2	Control 2 Occipital Ctx	24.7
AD 2 Temporal Ctx	35.4	Control 3 Occipital Ctx	43.2
AD 3 Temporal Ctx	48.3	Control 4 Occipital Ctx	10.4
AD 4 Temporal Ctx	36.9	Control (Path) 1 Occipital Ctx	95.3
AD 5 Inf Temporal Ctx	74.7	Control (Path) 2 Occipital Ctx	7.2
AD 5 SupTemporal Ctx	65.5	Control (Path) 3 Occipital Ctx	1.4
AD 6 Inf Temporal Ctx	85.9	Control (Path) 4 Occipital Ctx	25.7
AD 6 Sup Temporal Ctx	49.0	Control 1 Parietal Ctx	10.6
Control 1 Temporal Ctx	8.4	Control 2 Parietal Ctx	100.0
Control 2 Temporal Ctx	42.9	Control 3 Parietal Ctx	14.1
Control 3 Temporal Ctx	23.0	Control (Path) 1 Parietal Ctx	47.0
Control 4 Temporal Ctx	31.0	Control (Path) 2 Parietal Ctx	12.4
Control (Path) 1 Temporal Ctx	62.4	Control (Path) 3 Parietal Ctx	4.8
Control (Path) 2 Temporal Ctx	42.6	Control (Path) 4 Parietal Ctx	45.7

Table EC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3295, Run 215669651	Tissue Name	Rel. Exp.(%) Ag3295, Run 215669651
Adipose	0.2	Renal ca. TK-10	18.2
Melanoma* Hs688(A).T	0.1	Bladder	0.7
Melanoma* Hs688(B).T	0.4	Gastric ca. (liver met.) NCI-N87	4.3

Melanoma* M14	2.6	Gastric ca. KATO III	2.3
Melanoma* LOXIMVI	0.1	Colon ca. SW-948	0.2
Melanoma* SK-MEL-5	1.3	Colon ca. SW480	3.2
Squamous cell carcinoma SCC-4	0.5	Colon ca.* (SW480 met) SW620	0.8
Testis Pool	0.5	Colon ca. HT29	29.1
Prostate ca.* (bone met) PC-3	0.9	Colon ca. HCT-116	1.3
Prostate Pool	3.6	Colon ca. CaCo-2	4.9
Placenta	1.0	Colon cancer tissue	1.3
Uterus Pool	1.4	Colon ca. SW1116	0.7
Ovarian ca. OVCAR-3	0.2	Colon ca. Colo-205	0.6
Ovarian ca. SK-OV-3	0.9	Colon ca. SW-48	0.4
Ovarian ca. OVCAR-4	0.3	Colon Pool	0.9
Ovarian ca. OVCAR-5	4.2	Small Intestine Pool	1.2
Ovarian ca. IGROV-1	0.4	Stomach Pool	0.1
Ovarian ca. OVCAR-8	0.9	Bone Marrow Pool	2.9
Ovary	0.2	Fetal Heart	0.1
Breast ca. MCF-7	0.4	Heart Pool	0.0
Breast ca. MDA-MB-231	0.6	Lymph Node Pool	0.1
Breast ca. BT 549	2.9	Fetal Skeletal Muscle	0.1
Breast ca. T47D	20.4	Skeletal Muscle Pool	0.5
Breast ca. MDA-N	2.0	Spleen Pool	0.5
Breast Pool	0.4	Thymus Pool	0.5
Trachea	12.5	CNS cancer (glio/astro) U87-MG	3.4
Lung	0.3	CNS cancer (glio/astro) U-118-MG	0.4
Fetal Lung	0.5	CNS cancer (neuro;met) SK-N-AS	0.6
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.1
Lung ca. LX-1	2.0	CNS cancer (astro) SNB-75	2.2
Lung ca. NCI-H146	0.6	CNS cancer (glio) SNB-19	1.3
Lung ca. SHP-77	1.4	CNS cancer (glio) SF-295	3.7
Lung ca. A549	27.4	Brain (Amygdala) Pool	0.8
Lung ca. NCI-H526	0.2	Brain (cerebellum)	3.3
Lung ca. NCI-H23	3.1	Brain (fetal)	1.5
Lung ca. NCI-H460	2.7	Brain (Hippocampus) Pool	0.5
Lung ca. HOP-62	0.2	Cerebral Cortex Pool	0.6
Lung ca. NCI-H522	4.3	Brain (Substantia nigra) Pool	0.4
Liver	0.4	Brain (Thalamus) Pool	0.8
Fetal Liver	1.1	Brain (whole)	0.5
Liver ca. HepG2	42.9	Spinal Cord Pool	1.1
Kidney Pool	1.0	Adrenal Gland	0.2
Fetal Kidney	0.5	Pituitary gland Pool	0.1
Renal ca. 786-0	0.3	Salivary Gland	100.0
Renal ca. A498	5.1	Thyroid (female)	0.1
Renal ca. ACHN	0.4	Pancreatic ca. CAPAN2	2.8
Renal ca. UO-31	0.3	Pancreas Pool	0.7

Table ED. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3295, Run 164331710	Tissue Name	Rel. Exp.(%) Ag3295, Run 164331710
Secondary Th1 act	0.8	HUVEC IL-1beta	0.0
Secondary Th2 act	23.8	HUVEC IFN gamma	3.2

Secondary Tr1 act	11.9	HUVEC TNF alpha + IFN gamma	3.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	2.4	HUVEC IL-11	0.0
Secondary Tr1 rest	3.0	Lung Microvascular EC none	1.8
Primary Th1 act	12.5	Lung Microvascular EC TNFalpha + IL-1beta	3.7
Primary Th2 act	47.0	Microvascular Dermal EC none	4.0
Primary Tr1 act	30.1	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	9.5
Primary Th2 rest	1.4	Small airway epithelium none	100.0
Primary Tr1 rest	11.5	Small airway epithelium TNFalpha + IL-1beta	55.5
CD45RA CD4 lymphocyte act	0.7	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	5.0	Astrocytes rest	1.3
Secondary CD8 lymphocyte rest	5.9	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	8.8	KU-812 (Basophil) rest	2.5
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	3.9
2ry Th1/Th2/Tr1_anti-CD95 CH11	3.6	CCD1106 (Keratinocytes) none	2.7
LAK cells rest	17.7	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	14.9
LAK cells IL-2	6.2	Liver cirrhosis	11.1
LAK cells IL-2+IL-12	1.6	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	5.7	NCI-H292 none	1.4
LAK cells IL-2+ IL-18	9.9	NCI-H292 IL-4	3.1
LAK cells PMA/ionomycin	8.0	NCI-H292 IL-9	7.1
NK Cells IL-2 rest	3.3	NCI-H292 IL-13	1.0
Two Way MLR 3 day	9.9	NCI-H292 IFN gamma	1.6
Two Way MLR 5 day	8.7	HPAEC none	1.2
Two Way MLR 7 day	3.2	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	3.4
PBMC PWM	21.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	14.9	Lung fibroblast IL-4	0.5
Ramos (B cell) none	2.2	Lung fibroblast IL-9	3.7
Ramos (B cell) ionomycin	7.0	Lung fibroblast IL-13	1.5
B lymphocytes PWM	18.6	Lung fibroblast IFN gamma	1.6
B lymphocytes CD40L and IL-4	7.5	Dermal fibroblast CCD1070 rest	14.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	14.7
EOL-1 dbcAMP PMA/ionomycin	1.5	Dermal fibroblast CCD1070 IL-1 beta	2.7
Dendritic cells none	6.4	Dermal fibroblast IFN gamma	3.5
Dendritic cells LPS	11.0	Dermal fibroblast IL-4	6.6
Dendritic cells anti-CD40	8.4	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	6.7	Colon	41.5

Macrophages rest	4.9	Lung	16.7
Macrophages LPS	8.1	Thymus	0.0
HUVEC none	0.0	Kidney	13.9
HUVEC starved	1.8		

CNS_neurodegeneration_v1.0 Summary: Ag3295 This panel confirms the expression of this gene at low levels in the brain in an independent group of individuals (CTs = 33-35). However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see
 5 Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3295 Expression of the CG57611-01 gene is highest in the salivary gland (CT = 28). Therefore, expression of this gene may be used to distinguish salivary gland from the other samples on this panel. In general, expression of
 10 this gene appears to be higher in several cancer cell lines, including lung, breast, colon and liver cancer, when compared to normal tissues. Thus, therapeutic modulation of the activity of this gene or its protein product, using small molecule drugs, antibodies or protein therapeutics, may be of benefit in the treatment of lung, breast, colon and liver cancer. This gene encodes a protein with homology to CD22, a B lymphocyte-restricted adhesion molecule. Antibodies to
 15 the CD22 protein have been used as a therapeutic treatment for lymphomas (ref. 1), suggesting that the CG57611-01 protein may also be an attractive target for the treatment of leukemias and lymphomas.

This gene is also expressed at low but significant levels in the spinal cord, cerebellum, and amygdala. Therefore, this gene may play a role in central nervous system disorders such
 20 as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

References:

1. Rybak SM, Newton DL. Antibody targeted therapeutics for lymphoma: new focus on the CD22 antigen and RNA. Expert Opin Biol Ther 2001 Nov;1(6):995-1003

25 The approval of antibodies for cancer treatment has provoked increased interest in the development of new and improved antibody-mediated therapies. This emerging approach centres on targeting CD22 on human B-cells with a monoclonal antibody (mAb). Anti-CD22 antibodies conjugated to a cytotoxic RNase elicits potent and specific killing of the lymphoma cells in vitro and in human lymphoma models in severe combined immune deficiency (SCID)
 30 mice. RNA damage caused by RNases could be an important alternative to standard DNA

damaging chemotherapeutics. Moreover, targeted RNases may overcome problems of toxicity and immunogenicity associated with plant- or bacterial toxin-containing immunotoxins.

Panel 4D Summary: Ag3295 Expression of this gene is highest in small airway epithelium, irrespective of treatment (CTs = 31-32). Therefore, modulation of the expression or activity of the protein encoded by this transcript through the application of small molecule therapeutics may be useful in the treatment of asthma, COPD, and emphysema. Low but significant expression of this gene is seen in a number of samples on this panel. Expression of this gene appears to be higher in activated T cells than in resting T cells, suggesting that expression of this gene could be used to distinguish these two types of T cells.

NOV8

Expression of gene NOV8a/CG57452-01 and NOV8b/CG57452-02 was assessed using the primer-probe sets Ag3243 and Ag878, described in Tables FA and FB. Results of the RTQ-PCR runs are shown in Tables FC, FD, FE, FF, FG and FH. Please note that the CG57452-02 is only recognized by the Ag878 primer-probe set.

Table FA. Probe Name Ag3243

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ccatttcggacagtctcaatt-3'	21	1313	270
Probe	TET-5'-cctcacctttaagaatagtagctctggaca-3'-TAMRA	30	1337	271
Reverse	5'-aggtgaagctctgggtctttt-3'	21	1383	272

Table FB. Probe Name Ag878

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-agccctgtgtttttattgatga-3'	22	1745	273
Probe	TET-5'-cctgagccccaacaaggatttcatat-3'-TAMRA	26	1710	274
Reverse	5'-cagacgaagggtcaaatgg-3'	19	1682	275

Table FC. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3243, Run 210037850	Tissue Name	Rel. Exp.(%) Ag3243, Run 210037850
AD 1 Hippo	33.2	Control (Path) 3 Temporal Ctx	18.7
AD 2 Hippo	49.7	Control (Path) 4 Temporal Ctx	74.7
AD 3 Hippo	30.8	AD 1 Occipital Ctx	33.9
AD 4 Hippo	25.3	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	52.1	AD 3 Occipital Ctx	8.2
AD 6 Hippo	49.7	AD 4 Occipital Ctx	35.6
Control 2 Hippo	97.3	AD 5 Occipital Ctx	14.0
Control 4 Hippo	31.9	AD 6 Occipital Ctx	26.4
Control (Path) 3 Hippo	30.4	Control 1 Occipital Ctx	4.9
AD 1 Temporal Ctx	48.0	Control 2 Occipital Ctx	35.6
AD 2 Temporal Ctx	38.4	Control 3 Occipital Ctx	24.8

AD 3 Temporal Ctx	16.6	Control 4 Occipital Ctx	17.0
AD 4 Temporal Ctx	51.4	Control (Path) 1 Occipital Ctx	100.0
AD 5 Inf Temporal Ctx	51.4	Control (Path) 2 Occipital Ctx	35.6
AD 5 SupTemporal Ctx	80.1	Control (Path) 3 Occipital Ctx	6.1
AD 6 Inf Temporal Ctx	32.8	Control (Path) 4 Occipital Ctx	43.8
AD 6 Sup Temporal Ctx	32.5	Control 1 Parietal Ctx	19.8
Control 1 Temporal Ctx	43.8	Control 2 Parietal Ctx	52.1
Control 2 Temporal Ctx	26.1	Control 3 Parietal Ctx	9.7
Control 3 Temporal Ctx	42.3	Control (Path) 1 Parietal Ctx	62.4
Control 4 Temporal Ctx	26.1	Control (Path) 2 Parietal Ctx	50.3
Control (Path) 1 Temporal Ctx	93.3	Control (Path) 3 Parietal Ctx	10.9
Control (Path) 2 Temporal Ctx	77.9	Control (Path) 4 Parietal Ctx	46.7

Table FD. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3243, Run 214693632	Tissue Name	Rel. Exp.(%) Ag3243, Run 214693632
Adipose	0.0	Renal ca. TK-10	0.0
Melanoma* Hs688(A).T	0.0	Bladder	0.9
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	1.7	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.5	Colon ca. SW480	0.7
Squamous cell carcinoma SCC-4	0.0	Colon ca.* (SW480 met) SW620	0.0
Testis Pool	3.4	Colon ca. HT29	0.0
Prostate ca.* (bone met) PC-3	0.7	Colon ca. HCT-116	0.0
Prostate Pool	0.0	Colon ca. CaCo-2	0.0
Placenta	0.0	Colon cancer tissue	0.2
Uterus Pool	0.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.8	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	8.1	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	0.0	Colon Pool	0.2
Ovarian ca. OVCAR-5	0.0	Small Intestine Pool	5.3
Ovarian ca. IGROV-1	0.0	Stomach Pool	0.3
Ovarian ca. OVCAR-8	2.8	Bone Marrow Pool	0.0
Ovary	0.5	Fetal Heart	1.5
Breast ca. MCF-7	0.0	Heart Pool	0.3
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	0.0
Breast ca. BT 549	0.2	Fetal Skeletal Muscle	1.4
Breast ca. T47D	0.4	Skeletal Muscle Pool	0.0
Breast ca. MDA-N	0.0	Spleen Pool	9.4
Breast Pool	0.8	Thymus Pool	2.9
Trachea	0.3	CNS cancer (glio/astro) U87-MG	3.1
Lung	0.0	CNS cancer (glio/astro) U-118-MG	20.9

Fetal Lung	100.0	CNS cancer (neuro;met) SK-N-AS	0.7
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	0.0	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	2.5	CNS cancer (glio) SNB-19	0.0
Lung ca. SHP-77	0.2	CNS cancer (glio) SF-295	0.0
Lung ca. A549	0.3	Brain (Amygdala) Pool	38.4
Lung ca. NCI-H526	0.0	Brain (cerebellum)	5.1
Lung ca. NCI-H23	1.4	Brain (fetal)	11.9
Lung ca. NCI-H460	16.2	Brain (Hippocampus) Pool	42.9
Lung ca. HOP-62	0.4	Cerebral Cortex Pool	44.8
Lung ca. NCI-H522	1.1	Brain (Substantia nigra) Pool	28.5
Liver	0.0	Brain (Thalamus) Pool	54.3
Fetal Liver	0.0	Brain (whole)	32.8
Liver ca. HepG2	0.0	Spinal Cord Pool	32.1
Kidney Pool	0.0	Adrenal Gland	26.2
Fetal Kidney	73.2	Pituitary gland Pool	17.9
Renal ca. 786-0	0.0	Salivary Gland	0.0
Renal ca. A498	0.0	Thyroid (female)	0.0
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.5	Pancreas Pool	0.2

Table FE. Panel 1.2

Tissue Name	Rel. Exp.(%) Ag878, Run 118826261	Tissue Name	Rel. Exp.(%) Ag878, Run 118826261
Endothelial cells	4.0	Renal ca. 786-0	0.0
Heart (Fetal)	2.8	Renal ca. A498	0.3
Pancreas	6.5	Renal ca. RXF 393	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. ACHN	0.1
Adrenal Gland	68.8	Renal ca. UO-31	0.2
Thyroid	1.1	Renal ca. TK-10	0.0
Salivary gland	5.7	Liver	4.6
Pituitary gland	100.0	Liver (fetal)	0.6
Brain (fetal)	73.7	Liver ca. (hepatoblast) HepG2	0.0
Brain (whole)	53.2	Lung	27.2
Brain (amygdala)	46.7	Lung (fetal)	20.7
Brain (cerebellum)	20.2	Lung ca. (small cell) LX-1	0.1
Brain (hippocampus)	46.3	Lung ca. (small cell) NCI-H69	8.3
Brain (thalamus)	28.9	Lung ca. (s.cell var.) SHP-77	0.0
Cerebral Cortex	45.7	Lung ca. (large cell) NCI-H460	28.7
Spinal cord	27.4	Lung ca. (non-sm. cell) A549	1.0
glio/astro U87-MG	4.3	Lung ca. (non-s.cell) NCI-H23	0.8
glio/astro U-118-MG	8.3	Lung ca. (non-s.cell) HOP-62	1.9
astrocytoma SW1783	0.5	Lung ca. (non-s.cl) NCI-H522	5.7
neuro*; met SK-N-AS	9.2	Lung ca. (squam.) SW 900	0.1
astrocytoma SF-539	0.7	Lung ca. (squam.) NCI-H596	32.3
astrocytoma SNB-75	0.0	Mammary gland	6.4

glioma SNB-19	3.9	Breast ca. * (pl.ef) MCF-7	0.0
glioma U251	10.4	Breast ca. * (pl.ef) MDA-MB-231	0.0
glioma SF-295	2.4	Breast ca. * (pl. ef) T47D	5.3
Heart	16.2	Breast ca. BT-549	1.2
Skeletal Muscle	3.9	Breast ca. MDA-N	0.4
Bone marrow	0.0	Ovary	7.7
Thymus	0.8	Ovarian ca. OVCAR-3	12.2
Spleen	3.6	Ovarian ca. OVCAR-4	0.0
Lymph node	24.0	Ovarian ca. OVCAR-5	5.1
Colorectal Tissue	0.3	Ovarian ca. OVCAR-8	1.9
Stomach	5.7	Ovarian ca. IGROV-1	0.8
Small intestine	6.2	Ovarian ca. (ascites) SK-OV-3	12.5
Colon ca. SW480	0.3	Uterus	2.2
Colon ca. * SW620 (SW480 met)	0.0	Placenta	3.3
Colon ca. HT29	0.3	Prostate	0.5
Colon ca. HCT-116	0.0	Prostate ca. * (bone met) PC-3	4.1
Colon ca. CaCo-2	0.4	Testis	14.7
Colon ca. Tissue (ODO3866)	2.6	Melanoma Hs688(A).T	0.1
Colon ca. HCC-2998	0.0	Melanoma* (met) Hs688(B).T	0.9
Gastric ca. * (liver met) NCI-N87	0.0	Melanoma UACC-62	20.3
Bladder	4.9	Melanoma M14	1.4
Trachea	0.7	Melanoma LOX IMVI	5.6
Kidney	28.3	Melanoma* (met) SK-MEL-5	0.2
Kidney (fetal)	33.7		

Table FF. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag3243, Run 174443356	Tissue Name	Rel. Exp.(%) Ag3243, Run 174443356
Normal Colon	0.0	Kidney Margin (OD04348)	20.2
Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	0.0
Colon Margin (OD06064)	0.0	Kidney normal adjacent tissue (OD06204E)	5.2
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	0.0
Colon Margin (OD06159)	0.0	Kidney Margin (OD04450-03)	34.2
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-05)	0.0	Kidney Margin 8120614	1.7
CC Gr.2 ascend colon (ODO3921)	0.0	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	0.0
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	3.4
Colon mets to lung (OD04451-01)	8.3	Normal Uterus	0.0
Lung Margin (OD04451-02)	100.0	Uterine Cancer 064011	0.0
Normal Prostate	0.0	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer 064010	0.0

		TNFalpha + IL-1beta	
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	0.0
LAK cells IL-2+IL-12	0.0	NCI-H292 none	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 IL-4	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-9	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-13	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 3 day	0.0	HPAEC none	0.0
Two Way MLR 5 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
Two Way MLR 7 day	0.0	Lung fibroblast none	0.0
PBMC rest	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PWM	0.0	Lung fibroblast IL-4	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-13	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes PWM	0.0	Dermal fibroblast CCD1070 rest	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells none	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells LPS	0.0	Dermal Fibroblasts rest	0.0
Dendritic cells anti-CD40	0.0	Neutrophils TNFa+LPS	0.0
Monocytes rest	0.0	Neutrophils rest	0.0
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	7.2
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	100.0
HUVEC starved	0.0		

Table FH. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3243, Run 164390552	Tissue Name	Rel. Exp.(%) Ag3243, Run 164390552
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Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	0.0
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0

Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	3.2
Macrophages rest	0.0	Lung	18.2
Macrophages LPS	0.0	Thymus	100.0
HUVEC none	0.0	Kidney	3.8
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag3243 This panel confirms the expression of the CG57452-01 gene at low levels in the brain in an independent group of individuals. Interestingly, expression of this gene appears to be slightly down-regulated in the temporal cortex of Alzheimer's disease patients. Therefore, up-regulation of this gene or its protein product may be of use in reversing the dementia/memory loss and neuronal death associated with Alzheimer's disease.

General_screening_panel_v1.4 Summary: Ag3243 Expression of the CG57452-01 gene is highest in fetal lung (CT = 30) and fetal kidney (CT= 30.4). Therefore, expression of this gene may be used to distinguish these samples from the other samples on this panel.

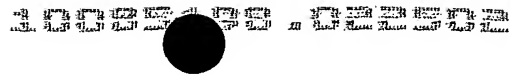
This gene is also expressed at moderate levels throughout the central nervous system (including in the amygdala, hippocampus, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord) and in one brain cancer line. This gene encodes a protein that is almost identical to protocadherin 15, a cell-adhesion molecule and member of the cadherin family of proteins. Cadherins can act as axon guidance and cell adhesion proteins, specifically during development and in the response to injury (ref. 1-2). Therefore, manipulation of levels of this protein may be of use in inducing a compensatory synaptogenic response to neuronal death in Alzheimer's disease, Parkinson's disease, Huntington's disease, spinocerebellar ataxia, progressive supranuclear palsy, ALS, head trauma, stroke, or any other disease/condition associated with neuronal loss.

Among tissues with metabolic or endocrine function, this gene is moderately expressed in pituitary gland and adrenal gland. This expression suggests that this gene product may play a role in normal metabolic and neuroendocrine function and that dysregulated expression of this gene may contribute to metabolic diseases (such as obesity and diabetes) or neuroendocrine disorders.

References:

1. Ranscht B. (2000) Cadherins: molecular codes for axon guidance and synapse formation. Int. J. Dev. Neurosci. 18: 643-651.

The formation of the myriad of neuronal connections within the vertebrate nervous system relies on expression of molecular tags that match extending axon populations with



synaptic target sites. Recent work suggests that cadherins, a group of calcium-dependent cell adhesion molecules, are candidates to serve such a role. The diversity of the cadherin family in the nervous system allows for a multitude of interactions to specify neuronal connections. Specific cadherin types demarcate subpopulations of developing axons that interconnect within neuronal circuits. Expression of different cadherin species at select synapse populations raises exciting prospects for this molecule class in controlling adhesive interactions during synaptogenesis and plasticity. Regulation of cadherin-mediated adhesive strength is an attractive mechanism to explain the different cadherin functions in axon growth and at synapses.

10 PMID: 10978842

2. Hilschmann N, Barnikol HU, Barnikol-Watanabe S, Gotz H, Kratzin H, Thinnies FP. The immunoglobulin-like genetic predetermination of the brain: the protocadherins, blueprint of the neuronal network. *Naturwissenschaften* 2001 Jan;88(1):2-12

The morphogenesis of the brain is governed by synaptogenesis. Synaptogenesis in turn is determined by cell adhesion molecules, which bridge the synaptic cleft and, by homophilic contact, decide which neurons are connected and which are not. Because of their enormous diversification in specificities, protocadherins (pcdh alpha, pcdh beta, pcdh gamma), a new class of cadherins, play a decisive role. Surprisingly, the genetic control of the protocadherins is very similar to that of the immunoglobulins. There are three sets of variable (V) genes followed by a corresponding constant (C) gene. Applying the rules of the immunoglobulin genes to the protocadherin genes leads, despite of this similarity, to quite different results in the central nervous system. The lymphocyte expresses one single receptor molecule specifically directed against an outside stimulus. In contrast, there are three specific recognition sites in each neuron, each expressing a different protocadherin. In this way, 4,950 different neurons arising from one stem cell form a neuronal network, in which homophilic contacts can be formed in 52 layers, permitting an enormous number of different connections and restraints between neurons. This network is one module of the central computer of the brain. Since the V-genes are generated during evolution and V-gene translocation during embryogenesis, outside stimuli have no influence on this network. The network is an inborn property of the protocadherin genes. Every circuit produced, as well as learning and memory, has to be based on this genetically predetermined network. This network is so universal that it can cope with everything, even the unexpected. In this respect the neuronal network resembles the recognition sites of the immunoglobulins.

PMID: 11261353

Panel 1.2 Summary: Ag878 The CG57452-01 gene encodes a protein that is almost identical to protocadherin 15, a cell-adhesion molecule and member of the cadherin family of proteins. Expression of this gene is highest in pituitary gland (CT = 28.0) and adrenal gland (CT = 28.6). Moderate expression of this gene is also seen in kidney, brain, and lung, consistent with what has been recently reported for the protocadherin 15 gene (ref 1). Expression of this gene is seen throughout the central nervous system, including in amygdala, hippocampus, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord. Mutations of the protocadherin gene PCDH15 have recently been shown to cause Usher syndrome type 1F (ref 2). Therefore, therapeutic modulation of the CG57452-01 protocadherin 15 protein may be of benefit in the treatment of Usher syndrome type 1F, deafness and retinitis pigmentosa. These results are consistent with what is observed in General_screening_panel_v1.4; please see this panel for additional information regarding the potential role of the protocadherin 15 gene in the CNS and metabolic/endocrine function.

References:

1. Murcia CL, Woychik RP. Expression of Pcdh15 in the inner ear, nervous system and various epithelia of the developing embryo. *Mech Dev* 2001 Jul;105(1-2):163-6.

Protocadherin 15 (Pcdh15) is associated with the Ames waltzer mutation in the mouse. Here we describe where the Pcdh15 gene is expressed at specific times during mouse development using RNA in situ hybridization. The expression of Pcdh15 is found in the sensory epithelium in the developing inner ear, in Rathke's pouch, and broadly throughout the brain with the highest level of expression being detected at embryonic day 16 (E16). Pcdh15 transcripts are also found in the developing eye, dorsal root ganglion, and the dorsal aspect of the neural tube, floor plate and ependymal cells adjacent to the neural canal. Additionally, expression is also detected in the developing glomeruli of the kidney, surface of the tongue, vibrissae, bronchi of the lung, and in the epithelium of the olfactory apparatus, gut and lung.

2. Ahmed ZM, Riazuddin S, Bernstein SL, Ahmed Z, Khan S, Griffith AJ, Morell RJ, Friedman TB, Riazuddin S, Wilcox ER. Mutations of the protocadherin gene PCDH15 cause Usher syndrome type 1F. *Am J Hum Genet* 2001 Jul;69(1):25-34

Human chromosome 10q21-22 harbors USH1F in a region of conserved synteny to mouse chromosome 10. This region of mouse chromosome 10 contains Pcdh15, encoding a protocadherin gene that is mutated in ames waltzer and causes deafness and vestibular dysfunction. Here we report two mutations of protocadherin 15 (PCDH15) found in two

families segregating Usher syndrome type 1F. A Northern blot probed with the PCDH15 cytoplasmic domain showed expression in the retina, consistent with its pathogenetic role in the retinitis pigmentosa associated with USH1F.

PMID: 11398101

5 **Panel 2.2 Summary:** Ag3243 Expression of this gene is seen at low levels in normal lung and kidney. Interestingly, expression is much lower in lung and kidney tumor samples than in the matched adjacent normal tissue. Therefore, expression of this gene could be used to distinguish normal lung and kidney from lung and kidney tumors. Furthermore, therapeutic modulation of the activity or amount of this gene product using protein therapeutics may be of benefit in the treatment of lung and kidney cancer.

15 **Panel 4.1D Summary:** Ag3243 The CG57452-01 gene is only expressed at detectable levels in the kidney (CT = 32.4). Therefore, antibody or small molecule therapies designed with the protein encoded for by this gene could modulate kidney function and be important in the treatment of inflammatory or autoimmune diseases that affect the kidney, including lupus and glomerulonephritis.

20 **Panel 4D Summary:** Ag3243 The CG57452-01 transcript is expressed at significant levels only in the thymus (CT = 33.1) in both runs. The putative protocadherin encoded for by the CG57452-01 gene could therefore play an important role in T cell development. Small molecule therapeutics, or antibody therapeutics designed against the protocadherin encoded for by this gene could be utilized to modulate immune function (T cell development) and be important for organ transplant, AIDS treatment or post chemotherapy immune reconstitution.

NOV9

25 Expression of NOV9/CG57625-01 was assessed using the primer-probe set Ag3297, described in Table GA. Results of the RTQ-PCR runs are shown in Tables GB, GC, GD and GE.

Table GA. Probe Name Ag3297

Primers	Sequences	Length	Start Position
Forward	5'-tgtgaatgtggaggatgctaa-3'	21	4696
Probe	TET-5'-tgatcacagtccttattttaccaacca-3'-TAMRA	28	4717
Reverse	5'-gattcaaacacagacgcttca-3'	21	4750

Table GB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3297, Run 210063001	Tissue Name	Rel. Exp.(%) Ag3297, Run 210063001
AD 1 Hippo	4.5	Control (Path) 3 Temporal	1.7

		Ctx	
AD 2 Hippo	10.2	Control (Path) 4 Temporal Ctx	18.4
AD 3 Hippo	2.3	AD 1 Occipital Ctx	9.3
AD 4 Hippo	2.1	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	100.0	AD 3 Occipital Ctx	2.5
AD 6 Hippo	22.1	AD 4 Occipital Ctx	12.1
Control 2 Hippo	19.1	AD 5 Occipital Ctx	32.1
Control 4 Hippo	3.2	AD 6 Occipital Ctx	44.8
Control (Path) 3 Hippo	2.6	Control 1 Occipital Ctx	0.5
AD 1 Temporal Ctx	4.5	Control 2 Occipital Ctx	43.5
AD 2 Temporal Ctx	16.7	Control 3 Occipital Ctx	11.5
AD 3 Temporal Ctx	1.5	Control 4 Occipital Ctx	2.4
AD 4 Temporal Ctx	12.6	Control (Path) 1 Occipital Ctx	49.7
AD 5 Inf Temporal Ctx	72.7	Control (Path) 2 Occipital Ctx	10.0
AD 5 SupTemporal Ctx	35.8	Control (Path) 3 Occipital Ctx	0.6
AD 6 Inf Temporal Ctx	21.3	Control (Path) 4 Occipital Ctx	11.3
AD 6 Sup Temporal Ctx	27.7	Control 1 Parietal Ctx	4.3
Control 1 Temporal Ctx	3.1	Control 2 Parietal Ctx	25.0
Control 2 Temporal Ctx	22.1	Control 3 Parietal Ctx	11.7
Control 3 Temporal Ctx	9.9	Control (Path) 1 Parietal Ctx	51.1
Control 4 Temporal Ctx	5.9	Control (Path) 2 Parietal Ctx	22.4
Control (Path) 1 Temporal Ctx	46.3	Control (Path) 3 Parietal Ctx	1.8
Control (Path) 2 Temporal Ctx	27.7	Control (Path) 4 Parietal Ctx	24.7

Table GC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3297, Run 215669728	Tissue Name	Rel. Exp.(%) Ag3297, Run 215669728
Adipose	0.9	Renal ca. TK-10	0.0
Melanoma* Hs688(A).T	1.5	Bladder	1.1
Melanoma* Hs688(B).T	3.8	Gastric ca. (liver met.) NCI-N87	6.9
Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	0.0	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	0.0
Squamous cell carcinoma SCC-4	0.0	Colon ca.* (SW480 met) SW620	0.0
Testis Pool	2.9	Colon ca. HT29	0.0
Prostate ca.* (bone met) PC-3	0.0	Colon ca. HCT-116	0.0
Prostate Pool	6.8	Colon ca. CaCo-2	0.0
Placenta	0.1	Colon cancer tissue	0.7
Uterus Pool	0.9	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	4.8	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	1.0	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	8.7	Colon Pool	1.7
Ovarian ca. OVCAR-5	0.2	Small Intestine Pool	1.8

Ovarian ca. IGROV-1	1.8	Stomach Pool	0.9
Ovarian ca. OVCAR-8	0.9	Bone Marrow Pool	0.5
Ovary	0.6	Fetal Heart	1.6
Breast ca. MCF-7	0.0	Heart Pool	0.7
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	5.2
Breast ca. BT 549	0.0	Fetal Skeletal Muscle	0.5
Breast ca. T47D	0.2	Skeletal Muscle Pool	0.2
Breast ca. MDA-N	1.2	Spleen Pool	0.2
Breast Pool	1.2	Thymus Pool	1.7
Trachea	0.6	CNS cancer (glio/astro) U87-MG	0.0
Lung	1.4	CNS cancer (glio/astro) U-118-MG	0.2
Fetal Lung	99.3	CNS cancer (neuro;met) SK-N-AS	0.0
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	2.0
Lung ca. LX-1	0.0	CNS cancer (astro) SNB-75	6.9
Lung ca. NCI-H146	0.1	CNS cancer (glio) SNB-19	1.9
Lung ca. SHP-77	7.0	CNS cancer (glio) SF-295	0.0
Lung ca. A549	2.0	Brain (Amygdala) Pool	14.3
Lung ca. NCI-H526	40.6	Brain (cerebellum)	3.4
Lung ca. NCI-H23	0.6	Brain (fetal)	100.0
Lung ca. NCI-H460	0.0	Brain (Hippocampus) Pool	14.7
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	23.8
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	15.2
Liver	0.1	Brain (Thalamus) Pool	21.3
Fetal Liver	1.4	Brain (whole)	23.3
Liver ca. HepG2	0.0	Spinal Cord Pool	7.5
Kidney Pool	3.4	Adrenal Gland	0.2
Fetal Kidney	12.3	Pituitary gland Pool	1.7
Renal ca. 786-0	0.1	Salivary Gland	0.0
Renal ca. A498	0.9	Thyroid (female)	0.1
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.5	Pancreas Pool	0.5

Table GD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3297, Run 164633943	Tissue Name	Rel. Exp.(%) Ag3297, Run 164633943
Secondary Th1 act	0.1	HUVEC IL-1beta	0.1
Secondary Th2 act	0.2	HUVEC IFN gamma	1.3
Secondary Tr1 act	0.4	HUVEC TNF alpha + IFN gamma	0.5
Secondary Th1 rest	0.4	HUVEC TNF alpha + IL4	0.4
Secondary Th2 rest	0.0	HUVEC IL-11	0.2
Secondary Tr1 rest	0.1	Lung Microvascular EC none	0.6
Primary Th1 act	0.1	Lung Microvascular EC TNFalpha + IL-1beta	0.1
Primary Th2 act	0.5	Microvascular Dermal EC none	1.2
Primary Tr1 act	0.4	Microvascular Dermal EC TNFalpha + IL-1beta	0.2
Primary Th1 rest	0.3	Bronchial epithelium TNFalpha + IL1beta	0.8
Primary Th2 rest	0.1	Small airway epithelium none	0.7
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	1.9
CD45RA CD4 lymphocyte	0.2	Coronary artery SMC rest	2.2

act			
CD45RO CD4 lymphocyte act	0.1	Coronary artery SMC TNFalpha + IL-1beta	2.3
CD8 lymphocyte act	0.1	Astrocytes rest	100.0
Secondary CD8 lymphocyte rest	1.1	Astrocytes TNFalpha + IL-1beta	28.9
Secondary CD8 lymphocyte act	1.6	KU-812 (Basophil) rest	2.9
CD4 lymphocyte none	0.4	KU-812 (Basophil) PMA/ionomycin	15.2
2ry Th1/Th2/Tr1_anti-CD95 CH11	1.5	CCD1106 (Keratinocytes) none	0.1
LAK cells rest	0.4	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.5
LAK cells IL-2	1.7	Liver cirrhosis	2.6
LAK cells IL-2+IL-12	1.4	Lupus kidney	2.0
LAK cells IL-2+IFN gamma	3.5	NCI-H292 none	1.0
LAK cells IL-2+ IL-18	1.1	NCI-H292 IL-4	4.7
LAK cells PMA/ionomycin	0.1	NCI-H292 IL-9	1.1
NK Cells IL-2 rest	0.8	NCI-H292 IL-13	1.7
Two Way MLR 3 day	0.3	NCI-H292 IFN gamma	0.6
Two Way MLR 5 day	1.0	HPAEC none	0.6
Two Way MLR 7 day	0.4	HPAEC TNF alpha + IL-1 beta	0.2
PBMC rest	0.3	Lung fibroblast none	8.7
PBMC PWM	1.0	Lung fibroblast TNF alpha + IL-1 beta	2.3
PBMC PHA-L	1.0	Lung fibroblast IL-4	18.7
Ramos (B cell) none	0.7	Lung fibroblast IL-9	18.8
Ramos (B cell) ionomycin	2.2	Lung fibroblast IL-13	14.7
B lymphocytes PWM	1.2	Lung fibroblast IFN gamma	12.2
B lymphocytes CD40L and IL-4	2.1	Dermal fibroblast CCD1070 rest	18.4
EOL-1 dbcAMP	0.5	Dermal fibroblast CCD1070 TNF alpha	16.2
EOL-1 dbcAMP PMA/ionomycin	0.4	Dermal fibroblast CCD1070 IL-1 beta	3.1
Dendritic cells none	0.4	Dermal fibroblast IFN gamma	0.3
Dendritic cells LPS	0.3	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	1.3	IBD Colitis 2	1.2
Monocytes rest	0.4	IBD Crohn's	0.5
Monocytes LPS	0.3	Colon	0.3
Macrophages rest	0.4	Lung	5.5
Macrophages LPS	0.7	Thymus	2.2
HUVEC none	0.8	Kidney	4.4
HUVEC starved	6.9		

Table GE. Panel CNS_1.1

Tissue Name	Rel. Exp.(%) Ag3297, Run 204173323	Tissue Name	Rel. Exp.(%) Ag3297, Run 204173323
Cing Gyr Depression2	5.1	BA17 PSP2	14.9
Cing Gyr Depression	10.1	BA17 PSP	46.3
Cing Gyr PSP2	1.5	BA17 Huntington's2	10.1
Cing Gyr PSP	11.8	BA17 Huntington's	32.3
Cing Gyr Huntington's2	13.4	BA17 Parkinson's2	54.7
Cing Gyr Huntington's	48.3	BA17 Parkinson's	37.6

Cing Gyr Parkinson's2	37.4	BA17 Alzheimer's2	7.0
Cing Gyr Parkinson's	47.3	BA17 Control2	48.3
Cing Gyr Alzheimer's2	4.5	BA17 Control	69.3
Cing Gyr Alzheimer's	16.3	BA9 Depression2	6.6
Cing Gyr Control2	30.8	BA9 Depression	9.2
Cing Gyr Control	66.0	BA9 PSP2	6.5
Temp Pole Depression2	5.6	BA9 PSP	18.4
Temp Pole PSP2	3.0	BA9 Huntington's2	8.7
Temp Pole PSP	4.4	BA9 Huntington's	61.6
Temp Pole Huntington's	22.1	BA9 Parkinson's2	64.6
Temp Pole Parkinson's2	24.8	BA9 Parkinson's	46.7
Temp Pole Parkinson's	32.8	BA9 Alzheimer's2	11.3
Temp Pole Alzheimer's2	3.3	BA9 Alzheimer's	7.4
Temp Pole Alzheimer's	5.1	BA9 Control2	69.3
Temp Pole Control2	51.8	BA9 Control	27.4
Temp Pole Control	27.5	BA7 Depression	10.9
Glob Palladus Depression	3.6	BA7 PSP2	27.9
Glob Palladus PSP2	5.5	BA7 PSP	56.3
Glob Palladus PSP	6.7	BA7 Huntington's2	21.3
Glob Palladus Parkinson's2	11.7	BA7 Huntington's	49.7
Glob Palladus Parkinson's	97.9	BA7 Parkinson's2	50.7
Glob Palladus Alzheimer's2	10.9	BA7 Parkinson's	20.3
Glob Palladus Alzheimer's	9.8	BA7 Alzheimer's2	4.3
Glob Palladus Control2	24.5	BA7 Control2	25.3
Glob Palladus Control	23.2	BA7 Control	45.4
Sub Nigra Depression2	5.9	BA4 Depression2	6.4
Sub Nigra Depression	3.3	BA4 Depression	14.5
Sub Nigra PSP2	5.1	BA4 PSP2	36.3
Sub Nigra Huntington's2	5.8	BA4 PSP	12.0
Sub Nigra Huntington's	74.2	BA4 Huntington's2	5.4
Sub Nigra Parkinson's2	39.5	BA4 Huntington's	42.0
Sub Nigra Alzheimer's2	3.8	BA4 Parkinson's2	100.0
Sub Nigra Control2	12.7	BA4 Parkinson's	52.9
Sub Nigra Control	45.1	BA4 Alzheimer's2	3.0
BA17 Depression2	11.0	BA4 Control2	53.2
BA17 Depression	7.1	BA4 Control	36.3

CNS_neurodegeneration_v1.0 Summary: Ag3297 This panel confirms the expression of this gene at low levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3297 The CG57625-01 gene is expressed at low to moderate levels in many of the tissues on this panel, with the highest levels of expression in fetal brain and fetal lung (CT = 27.4). Interestingly, the levels of

expression are significantly lower in the sample from adult lung (CT = 33.5) than in fetal lung. Therefore, expression of this gene can be used to distinguish fetal lung from adult lung.

This gene is expressed at low levels throughout the CNS, including in amygdala, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord. The CG57625-01 gene encodes a protein with homology to protocadherin, a cell-adhesion molecule and member of the cadherin family of proteins. Cadherins can act as axon guidance and cell adhesion proteins, specifically during development and in the response to injury (ref. 1-2). Therefore, manipulation of levels of this protein may be of use in inducing a compensatory synaptogenic response to neuronal death in Alzheimer's disease, Parkinson's disease, Huntington's disease, spinocerebellar ataxia, progressive supranuclear palsy, ALS, head trauma, stroke, or any other disease/condition associated with neuronal loss.

This gene is also expressed at low to moderate levels in a number of tissues with metabolic or endocrine function, including heart, gastrointestinal tract, fetal liver, pituitary gland, and adipose. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

Additionally, this gene is also expressed at significant levels in lung cancer, ovarian cancer, gastric cancer and melanoma cell lines. Hence expression of this gene could be used as a diagnostic marker for these types of cancers. Furthermore, therapeutic modulation of the activity of this gene or its protein product, using small molecule drugs, antibodies, or protein therapeutics, may be of use in the treatment of lung cancer, ovarian cancer, gastric cancer and melanoma.

References:

1. Ranscht B. (2000) Cadherins: molecular codes for axon guidance and synapse formation. *Int. J. Dev. Neurosci.* 18: 643-651.

The formation of the myriad of neuronal connections within the vertebrate nervous system relies on expression of molecular tags that match extending axon populations with synaptic target sites. Recent work suggests that cadherins, a group of calcium-dependent cell adhesion molecules, are candidates to serve such a role. The diversity of the cadherin family in the nervous system allows for a multitude of interactions to specify neuronal connections. Specific cadherin types demarcate subpopulations of developing axons that interconnect within neuronal circuits. Expression of different cadherin species at select synapse populations raises exciting prospects for this molecule class in controlling adhesive interactions during

synaptogenesis and plasticity. Regulation of cadherin-mediated adhesive strength is an attractive mechanism to explain the different cadherin functions in axon growth and at synapses.

PMID: 10978842

- 5 2. Hilschmann N, Barnikol HU, Barnikol-Watanabe S, Gotz H, Kratzin H, Thinnies FP. The immunoglobulin-like genetic predetermination of the brain: the protocadherins, blueprint of the neuronal network. *Naturwissenschaften* 2001 Jan;88(1):2-12

10 The morphogenesis of the brain is governed by synaptogenesis. Synaptogenesis in turn is determined by cell adhesion molecules, which bridge the synaptic cleft and, by homophilic contact, decide which neurons are connected and which are not. Because of their enormous diversification in specificities, protocadherins (pcdh alpha, pcdh beta, pcdh gamma), a new class of cadherins, play a decisive role. Surprisingly, the genetic control of the protocadherins is very similar to that of the immunoglobulins. There are three sets of variable (V) genes followed by a corresponding constant (C) gene. Applying the rules of the immunoglobulin genes to the protocadherin genes leads, despite of this similarity, to quite different results in the central nervous system. The lymphocyte expresses one single receptor molecule specifically directed against an outside stimulus. In contrast, there are three specific recognition sites in each neuron, each expressing a different protocadherin. In this way, 4,950 different neurons arising from one stem cell form a neuronal network, in which homophilic contacts can be formed in 52 layers, permitting an enormous number of different connections and restraints between neurons. This network is one module of the central computer of the brain. Since the V-genes are generated during evolution and V-gene translocation during embryogenesis, outside stimuli have no influence on this network. The network is an inborn property of the protocadherin genes. Every circuit produced, as well as learning and memory, has to be based on this genetically predetermined network. This network is so universal that it can cope with everything, even the unexpected. In this respect the neuronal network resembles the recognition sites of the immunoglobulins.

PMID: 11261353

30 **Panel 4D Summary:** Ag3297 Expression of the CG57625-01 gene is highest in resting astrocytes (CT = 28), consistent with the expression of this gene in the brain in General_screening_panel_v1.4. This gene is also moderately expressed in lung and dermal fibroblasts, irrespective of treatment. Therefore, therapeutic modulation of the activity of this gene or its protein product may be of benefit in the treatment of asthma, emphysema, and

psoriasis. Low levels of expression of this gene are detected in a number of other samples on this panel.

Panel CNS_1.1 Summary: Ag3297 This panel confirms the expression of this gene at low to moderate levels in the brain in an independent group of individuals. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

NOV10

Expression of NOV10/CG57553-01 was assessed using the primer-probe set Ag3283, described in Table HA. Results of the RTQ-PCR runs are shown in Tables HB, HC and HD.

10 Table HA. Probe Name Ag3283

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gcctccaatatgaaactcaaa-3'	22	461	276
Probe	TET-5'-tcctcagctacgagtaagtctgtctca-3'-TAMRA	28	504	277
Reverse	5'-cagaacctcaggtgtgattt-3'	22	532	278

Table HB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3283, Run 210060840	Tissue Name	Rel. Exp.(%) Ag3283, Run 210060840
AD 1 Hippo	13.3	Control (Path) 3 Temporal Ctx	4.5
AD 2 Hippo	14.1	Control (Path) 4 Temporal Ctx	44.1
AD 3 Hippo	15.4	AD 1 Occipital Ctx	19.1
AD 4 Hippo	7.6	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	76.8	AD 3 Occipital Ctx	15.1
AD 6 Hippo	65.1	AD 4 Occipital Ctx	22.7
Control 2 Hippo	25.2	AD 5 Occipital Ctx	41.8
Control 4 Hippo	10.7	AD 6 Occipital Ctx	26.4
Control (Path) 3 Hippo	13.8	Control 1 Occipital Ctx	6.2
AD 1 Temporal Ctx	34.9	Control 2 Occipital Ctx	35.8
AD 2 Temporal Ctx	40.3	Control 3 Occipital Ctx	23.7
AD 3 Temporal Ctx	9.2	Control 4 Occipital Ctx	11.1
AD 4 Temporal Ctx	18.4	Control (Path) 1 Occipital Ctx	90.1
AD 5 Inf Temporal Ctx	100.0	Control (Path) 2 Occipital Ctx	12.3
AD 5 Sup Temporal Ctx	51.1	Control (Path) 3 Occipital Ctx	5.3
AD 6 Inf Temporal Ctx	76.8	Control (Path) 4 Occipital Ctx	23.0
AD 6 Sup Temporal Ctx	93.3	Control 1 Parietal Ctx	2.9
Control 1 Temporal Ctx	6.7	Control 2 Parietal Ctx	65.1
Control 2 Temporal Ctx	36.3	Control 3 Parietal Ctx	18.3
Control 3 Temporal Ctx	13.1	Control (Path) 1 Parietal Ctx	52.1
Control 3 Temporal Ctx	8.7	Control (Path) 2 Parietal	28.7

		Ctx	
Control (Path) 1 Temporal Ctx	45.1	Control (Path) 3 Parietal Ctx	5.4
Control (Path) 2 Temporal Ctx	27.7	Control (Path) 4 Parietal Ctx	52.1

Table HC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3283, Run 216512996	Tissue Name	Rel. Exp.(%) Ag3283, Run 216512996
Adipose	8.3	Renal ca. TK-10	29.3
Melanoma* Hs688(A).T	5.0	Bladder	25.2
Melanoma* Hs688(B).T	9.7	Gastric ca. (liver met.) NCI-N87	40.9
Melanoma* M14	21.6	Gastric ca. KATO III	48.3
Melanoma* LOXIMVI	12.8	Colon ca. SW-948	9.1
Melanoma* SK-MEL-5	14.7	Colon ca. SW480	28.3
Squamous cell carcinoma SCC-4	8.4	Colon ca. * (SW480 met) SW620	21.2
Testis Pool	20.3	Colon ca. HT29	13.4
Prostate ca. * (bone met) PC-3	16.4	Colon ca. HCT-116	37.6
Prostate Pool	6.2	Colon ca. CaCo-2	14.2
Placenta	1.0	Colon cancer tissue	13.9
Uterus Pool	4.1	Colon ca. SW1116	2.6
Ovarian ca. OVCAR-3	30.6	Colon ca. Colo-205	10.8
Ovarian ca. SK-OV-3	61.6	Colon ca. SW-48	6.5
Ovarian ca. OVCAR-4	4.9	Colon Pool	15.5
Ovarian ca. OVCAR-5	28.5	Small Intestine Pool	21.5
Ovarian ca. IGROV-1	16.0	Stomach Pool	13.3
Ovarian ca. OVCAR-8	8.8	Bone Marrow Pool	5.4
Ovary	14.8	Fetal Heart	10.2
Breast ca. MCF-7	24.5	Heart Pool	7.9
Breast ca. MDA-MB-231	50.3	Lymph Node Pool	17.0
Breast ca. BT 549	100.0	Fetal Skeletal Muscle	6.2
Breast ca. T47D	47.3	Skeletal Muscle Pool	17.7
Breast ca. MDA-N	14.5	Spleen Pool	17.2
Breast Pool	19.8	Thymus Pool	20.6
Trachea	7.3	CNS cancer (glio/astro) U87-MG	37.4
Lung	7.5	CNS cancer (glio/astro) U-118-MG	49.7
Fetal Lung	37.6	CNS cancer (neuro;met) SK-N-AS	80.7
Lung ca. NCI-N417	4.6	CNS cancer (astro) SF-539	11.5
Lung ca. LX-1	41.8	CNS cancer (astro) SNB-75	36.3
Lung ca. NCI-H146	11.3	CNS cancer (glio) SNB-19	12.4
Lung ca. SHP-77	26.6	CNS cancer (glio) SF-295	29.5
Lung ca. A549	18.8	Brain (Amygdala) Pool	6.3
Lung ca. NCI-H526	13.9	Brain (cerebellum)	4.4
Lung ca. NCI-H23	31.4	Brain (fetal)	43.8
Lung ca. NCI-H460	17.6	Brain (Hippocampus) Pool	14.5
Lung ca. HOP-62	16.2	Cerebral Cortex Pool	11.4
Lung ca. NCI-H522	23.3	Brain (Substantia nigra) Pool	7.9
Liver	0.1	Brain (Thalamus) Pool	17.0
Fetal Liver	22.8	Brain (whole)	3.2

Liver ca. HepG2	21.5	Spinal Cord Pool	11.5
Kidney Pool	23.3	Adrenal Gland	4.0
Fetal Kidney	40.9	Pituitary gland Pool	3.8
Renal ca. 786-0	57.0	Salivary Gland	0.4
Renal ca. A498	2.3	Thyroid (female)	5.1
Renal ca. ACHN	11.3	Pancreatic ca. CAPAN2	51.1
Renal ca. UO-31	15.0	Pancreas Pool	22.2

Table HD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3283, Run 164634322	Tissue Name	Rel. Exp.(%) Ag3283, Run 164634322
Secondary Th1 act	6.9	HUVEC IL-1beta	7.2
Secondary Th2 act	7.3	HUVEC IFN gamma	10.7
Secondary Tr1 act	6.3	HUVEC TNF alpha + IFN gamma	2.9
Secondary Th1 rest	1.8	HUVEC TNF alpha + IL4	5.8
Secondary Th2 rest	3.4	HUVEC IL-11	3.5
Secondary Tr1 rest	4.7	Lung Microvascular EC none	8.8
Primary Th1 act	7.6	Lung Microvascular EC TNFalpha + IL-1beta	10.7
Primary Th2 act	5.5	Microvascular Dermal EC none	11.6
Primary Tr1 act	7.4	Microvascular Dermal EC TNFalpha + IL-1beta	6.6
Primary Th1 rest	23.0	Bronchial epithelium TNFalpha + IL1beta	7.8
Primary Th2 rest	17.9	Small airway epithelium none	1.0
Primary Tr1 rest	8.2	Small airway epithelium TNFalpha + IL-1beta	18.4
CD45RA CD4 lymphocyte act	4.9	Coronary artery SMC rest	2.5
CD45RO CD4 lymphocyte act	8.2	Coronary artery SMC TNFalpha + IL-1beta	2.8
CD8 lymphocyte act	5.8	Astrocytes rest	5.9
Secondary CD8 lymphocyte rest	3.2	Astrocytes TNFalpha + IL-1beta	2.4
Secondary CD8 lymphocyte act	6.8	KU-812 (Basophil) rest	4.3
CD4 lymphocyte none	2.5	KU-812 (Basophil) PMA/ionomycin	21.8
2ry Th1/Th2/Tr1_anti-CD95 CH11	6.5	CCD1106 (Keratinocytes) none	6.6
LAK cells rest	14.2	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	2.0
LAK cells IL-2	14.2	Liver cirrhosis	1.5
LAK cells IL-2+IL-12	7.4	Lupus kidney	1.5
LAK cells IL-2+IFN gamma	13.8	NCI-H292 none	17.4
LAK cells IL-2+ IL-18	9.7	NCI-H292 IL-4	18.9
LAK cells PMA/ionomycin	5.0	NCI-H292 IL-9	23.5
NK Cells IL-2 rest	14.4	NCI-H292 IL-13	5.3
Two Way MLR 3 day	19.2	NCI-H292 IFN gamma	8.5
Two Way MLR 5 day	5.6	HPAEC none	6.3
Two Way MLR 7 day	3.1	HPAEC TNF alpha + IL-1 beta	8.0
PBMC rest	7.4	Lung fibroblast none	4.7
PBMC PWM	24.8	Lung fibroblast TNF alpha + IL-1 beta	1.8
PBMC PHA-L	8.8	Lung fibroblast IL-4	10.4
Ramos (B cell) none	26.4	Lung fibroblast IL-9	6.7

Ramos (B cell) ionomycin	100.0	Lung fibroblast IL-13	6.5
B lymphocytes PWM	22.7	Lung fibroblast IFN gamma	7.2
B lymphocytes CD40L and IL-4	21.5	Dermal fibroblast CCD1070 rest	25.0
EOL-1 dbcAMP	15.3	Dermal fibroblast CCD1070 TNF alpha	56.3
EOL-1 dbcAMP PMA/ionomycin	27.7	Dermal fibroblast CCD1070 IL-1 beta	7.5
Dendritic cells none	13.5	Dermal fibroblast IFN gamma	2.8
Dendritic cells LPS	6.8	Dermal fibroblast IL-4	8.6
Dendritic cells anti-CD40	12.3	IBD Colitis 2	0.4
Monocytes rest	13.8	IBD Crohn's	1.8
Monocytes LPS	13.4	Colon	28.7
Macrophages rest	12.4	Lung	4.4
Macrophages LPS	10.3	Thymus	16.3
HUVEC none	7.3	Kidney	32.5
HUVEC starved	22.1		

CNS_neurodegeneration_v1.0 Summary: Ag3283 This panel confirms the expression of the CG57553-01 gene at low to moderate levels in the brain in an independent group of individuals. Interestingly, this gene appears to be slightly upregulated in the temporal cortex of Alzheimer's disease patients. Therefore, therapeutic modulation of the activity of this gene or its protein product may be of use to decrease neuronal death in the treatment of Alzheimer's disease or other neurological disorders.

General_screening_panel_v1.4 Summary: Ag3283 Expression of the CG57553-01 gene is highest in a breast cancer cell line (CT = 27.2). This gene is expressed at low to moderate levels in a number of tissues with metabolic or endocrine function, including adipose, adrenal gland, gastrointestinal tract, pancreas, skeletal muscle and thyroid. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes. Interestingly, this gene is differentially expressed in adult (CT = 36) vs fetal liver (CT = 29) and may be useful for distinguishing adult and fetal liver.

This gene is also expressed at moderate levels throughout the CNS, including in amygdala, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

There are also significant levels of expression in clusters of cell lines derived from melanoma, prostate, ovarian, brain, breast, pancreatic, gastric, and liver cancers. This observation suggests that expression of this gene may be associated with these cancers. Therefore, therapeutic modulation of the activity of this gene or its protein product might be of use in the treatment of these cancers.

Panel 4D Summary: Ag3283 The CG57553-01 gene is expressed at low to moderate levels in a number cell types within this panel, with highest expression in activated B cells (CT = 27.2). Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of rheumatic disease including rheumatoid arthritis, lupus, osteoarthritis, and hyperproliferative B cell disorders.

NOV11

Expression of gene NOV11a/CG57488-01 and variants NOV11B/CG57488-02 and NOV11C/CG57488-03 was assessed using the primer-probe sets Ag3254 and Ag3339, described in Tables IA and IB. Results of the RTQ-PCR runs are shown in Tables IC, ID and IE. Please note that variant CG57488-03 is only recognized by primer-probe set Ag3339.

Table IA. Probe Name Ag3254

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ctgtgcctgtggttaacatct-3'	22	5853	279
Probe	TET-5'-tgatcactccaggatattgacacgaa-3'-TAMRA	26	5892	280
Reverse	5'-accccgagaacatgtgagtaaga-3'	22	5931	281

Table IB. Probe Name Ag3339

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ggtcttctacgtcaggagagaat-3'	22	1806	282
Probe	TET-5'-cagtttgagtcgagaccttcttca-3'-TAMRA	26	1852	283
Reverse	5'-gctgaatacgtcactgaaacct-3'	22	1883	284

Table IC. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3254, Run 209990706	Rel. Exp.(%) Ag3339, Run 210139045	Tissue Name	Rel. Exp.(%) Ag3254, Run 209990706	Rel. Exp.(%) Ag3339, Run 210139045
AD 1 Hippo	0.0	19.1	Control (Path) 3 Temporal Ctx	28.9	6.2
AD 2 Hippo	38.2	70.7	Control (Path) 4 Temporal Ctx	0.0	3.7
AD 3 Hippo	7.3	9.1	AD 1 Occipital Ctx	0.0	17.7
AD 4 Hippo	12.1	5.4	AD 2 Occipital Ctx (Missing)	0.0	0.0
AD 5 Hippo	53.2	25.3	AD 3 Occipital Ctx	18.2	19.2
AD 6 Hippo	5.8	100.0	AD 4 Occipital Ctx	59.9	11.7
Control 2 Hippo	39.2	17.7	AD 5 Occipital Ctx	38.2	12.3
Control 4 Hippo	58.6	6.9	AD 6 Occipital Ctx	0.0	22.5
Control (Path) 3 Hippo	16.2	10.6	Control 1 Occipital Ctx	0.0	7.2
AD 1 Temporal Ctx	0.0	6.1	Control 2 Occipital Ctx	68.8	31.2
AD 2 Temporal Ctx	49.0	14.7	Control 3 Occipital Ctx	23.3	18.0

AD 3 Temporal Ctx	8.5	3.1	Control 4 Occipital Ctx	27.2	31.4
AD 4 Temporal Ctx	57.0	4.5	Control (Path) 1 Occipital Ctx	33.4	34.2
AD 5 Inf Temporal Ctx	89.5	53.6	Control (Path) 2 Occipital Ctx	11.7	4.6
AD 5 Sup Temporal Ctx	60.7	62.4	Control (Path) 3 Occipital Ctx	100.0	4.3
AD 6 Inf Temporal Ctx	0.0	31.6	Control (Path) 4 Occipital Ctx	0.0	10.4
AD 6 Sup Temporal Ctx	0.0	22.4	Control 1 Parietal Ctx	13.0	4.7
Control 1 Temporal Ctx	0.0	2.6	Control 2 Parietal Ctx	61.6	20.6
Control 2 Temporal Ctx	56.3	3.8	Control 3 Parietal Ctx	0.0	12.3
Control 3 Temporal Ctx	27.2	3.3	Control (Path) 1 Parietal Ctx	9.1	11.3
Control 3 Temporal Ctx	0.0	3.9	Control (Path) 2 Parietal Ctx	0.0	15.9
Control (Path) 1 Temporal Ctx	63.7	3.2	Control (Path) 3 Parietal Ctx	68.3	7.0
Control (Path) 2 Temporal Ctx	16.0	1.5	Control (Path) 4 Parietal Ctx	5.8	31.6

Table ID: General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3254, Run 214694852	Rel. Exp.(%) Ag3339, Run 215773747	Tissue Name	Rel. Exp.(%) Ag3254, Run 214694852	Rel. Exp.(%) Ag3339, Run 215773747
Adipose	0.1	0.1	Renal ca. TK-10	0.7	0.0
Melanoma* Hs688(A).T	0.2	0.0	Bladder	0.3	0.1
Melanoma* Hs688(B).T	0.3	0.0	Gastric ca. (liver met.) NCI-N87	4.9	0.0
Melanoma* M14	0.0	0.0	Gastric ca. KATO III	0.0	0.0
Melanoma* LOXIMVI	0.2	0.0	Colon ca. SW-948	0.0	0.0
Melanoma* SK- MEL-5	0.9	0.0	Colon ca. SW480	1.6	0.0
Squamous cell carcinoma SCC-4	0.4	0.0	Colon ca.* (SW480 met) SW620	5.3	0.1
Testis Pool	2.5	2.0	Colon ca. HT29	0.0	0.0
Prostate ca.* (bone met) PC-3	3.6	0.0	Colon ca. HCT-116	0.0	0.0
Prostate Pool	0.3	1.9	Colon ca. CaCo-2	0.0	0.2
Placenta	3.0	1.3	Colon cancer tissue	1.8	0.1
Uterus Pool	1.3	0.1	Colon ca. SW1116	0.0	0.0
Ovarian ca. OVCAR-3	1.8	0.2	Colon ca. Colo-205	0.0	0.0
Ovarian ca. SK- OV-3	2.4	0.7	Colon ca. SW-48	0.2	0.0
Ovarian ca. OVCAR-4	0.8	0.9	Colon Pool	5.7	0.7
Ovarian ca. OVCAR-5	1.5	1.8	Small Intestine Pool	22.4	0.8
Ovarian ca. IGROV-1	2.0	0.1	Stomach Pool	3.1	0.8
Ovarian ca. OVCAR-8	0.4	0.0	Bone Marrow Pool	3.8	0.3

Ovary	2.5	0.2	Fetal Heart	0.1	0.4
Breast ca. MCF-7	0.5	0.1	Heart Pool	1.9	0.4
Breast ca. MDA-MB-231	1.0	0.0	Lymph Node Pool	14.6	0.8
Breast ca. BT 549	0.0	0.1	Fetal Skeletal Muscle	0.2	0.2
Breast ca. T47D	6.4	7.6	Skeletal Muscle Pool	0.4	0.2
Breast ca. MDA-N	0.0	0.0	Spleen Pool	6.2	0.2
Breast Pool	7.0	1.1	Thymus Pool	4.1	1.0
Trachea	2.8	2.0	CNS cancer (glio/astro) U87-MG	0.0	0.0
Lung	0.3	0.0	CNS cancer (glio/astro) U-118-MG	0.0	0.0
Fetal Lung	7.5	17.0	CNS cancer (neuro;met) SK-N-AS	1.2	0.0
Lung ca. NCI-N417	0.0	0.0	CNS cancer (astro) SF-539	0.0	0.0
Lung ca. LX-1	26.4	0.1	CNS cancer (astro) SNB-75	0.0	0.0
Lung ca. NCI-H146	0.1	0.0	CNS cancer (glio) SNB-19	0.9	0.0
Lung ca. SHP-77	100.0	0.1	CNS cancer (glio) SF-295	0.0	0.0
Lung ca. A549	0.0	0.0	Brain (Amygdala) Pool	0.2	0.7
Lung ca. NCI-H526	0.0	0.0	Brain (cerebellum)	0.6	0.9
Lung ca. NCI-H23	2.1	100.0	Brain (fetal)	5.9	0.9
Lung ca. NCI-H460	0.0	0.1	Brain (Hippocampus) Pool	0.8	0.9
Lung ca. HOP-62	0.0	0.0	Cerebral Cortex Pool	0.1	0.5
Lung ca. NCI-H522	3.3	0.6	Brain (Substantia nigra) Pool	1.8	1.0
Liver	0.0	0.1	Brain (Thalamus) Pool	1.5	0.9
Fetal Liver	1.8	0.1	Brain (whole)	1.4	0.3
Liver ca. HepG2	0.6	0.0	Spinal Cord Pool	3.2	5.9
Kidney Pool	25.7	0.5	Adrenal Gland	4.2	0.6
Fetal Kidney	5.4	2.8	Pituitary gland Pool	0.5	0.1
Renal ca. 786-0	0.5	0.0	Salivary Gland	0.9	0.1
Renal ca. A498	0.3	0.0	Thyroid (female)	0.4	0.2
Renal ca. ACHN	0.1	0.0	Pancreatic ca. CAPAN2	0.0	0.1
Renal ca. UO-31	1.3	0.0	Pancreas Pool	6.4	1.1

Table IE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3254, Run 164391364	Rel. Exp.(%) Ag3339, Run 165221778	Tissue Name	Rel. Exp.(%) Ag3254, Run 164391364	Rel. Exp.(%) Ag3339, Run 165221778
Secondary Th1 act	0.0	0.0	HUVEC IL-1beta	0.0	1.4
Secondary Th2 act	0.0	0.0	HUVEC IFN gamma	0.0	0.0
Secondary Tr1 act	0.0	0.0	HUVEC TNF alpha + IFN gamma	0.0	0.0
Secondary Th1 rest	0.0	0.0	HUVEC TNF alpha + IL4	0.0	1.0
Secondary Th2 rest	0.0	0.0	HUVEC IL-11	0.0	1.4

Secondary Tr1 rest	0.0	0.0	Lung Microvascular EC none	0.0	0.0
Primary Th1 act	0.0	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0	0.0
Primary Th2 act	0.0	0.0	Microvascular Dermal EC none	0.0	0.0
Primary Tr1 act	0.0	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0	7.5
Primary Th1 rest	0.0	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0	6.7
Primary Th2 rest	0.0	1.2	Small airway epithelium none	0.0	0.0
Primary Tr1 rest	0.0	0.9	Small airway epithelium TNFalpha + IL-1beta	0.0	36.6
CD45RA CD4 lymphocyte act	0.0	0.0	Coronary artery SMC rest	0.0	0.0
CD45RO CD4 lymphocyte act	0.0	0.0	Coronary artery SMC TNFalpha + IL-1beta	0.0	0.0
CD8 lymphocyte act	0.0	0.0	Astrocytes rest	0.0	0.0
Secondary CD8 lymphocyte rest	0.0	0.0	Astrocytes TNFalpha + IL-1beta	0.0	0.0
Secondary CD8 lymphocyte act	0.0	0.0	KU-812 (Basophil) rest	0.0	1.9
CD4 lymphocyte none	0.0	5.7	KU-812 (Basophil) PMA/ionomycin	0.0	2.8
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	0.0	CCD1106 (Keratinocytes) none	0.0	0.0
LAK cells rest	0.0	1.1	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0	1.4
LAK cells IL-2	0.0	0.0	Liver cirrhosis	0.0	4.6
LAK cells IL-2+IL-12	0.0	0.0	Lupus kidney	0.0	32.1
LAK cells IL-2+IFN gamma	0.0	0.0	NCI-H292 none	0.0	0.0
LAK cells IL-2+ IL-18	0.0	0.7	NCI-H292 IL-4	0.0	1.3
LAK cells PMA/ionomycin	0.0	1.2	NCI-H292 IL-9	0.0	2.5
NK Cells IL-2 rest	0.0	3.0	NCI-H292 IL-13	0.0	0.0
Two Way MLR 3 day	0.0	2.7	NCI-H292 IFN gamma	0.0	0.0
Two Way MLR 5 day	0.0	0.0	HPAEC none	0.0	0.0
Two Way MLR 7 day	100.0	0.0	HPAEC TNF alpha + IL-1 beta	0.0	44.8
PBMC rest	0.0	16.8	Lung fibroblast none	0.0	0.0
PBMC PWM	0.0	2.4	Lung fibroblast TNF alpha + IL-1 beta	0.0	0.0
PBMC PHA-L	0.0	0.0	Lung fibroblast IL-4	0.0	0.0
Ramos (B cell) none	0.0	0.0	Lung fibroblast IL-9	0.0	0.0
Ramos (B cell) ionomycin	0.0	0.0	Lung fibroblast IL-13	0.0	0.0
B lymphocytes PWM	0.0	0.0	Lung fibroblast IFN gamma	0.0	0.0
B lymphocytes CD40L and IL-4	0.0	0.0	Dermal fibroblast CCD1070 rest	0.0	0.0
EOL-1 dbcAMP	0.0	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0	1.5
EOL-1 dbcAMP PMA/ionomycin	0.0	1.4	Dermal fibroblast CCD1070 IL-1 beta	0.0	0.0

Dendritic cells none	0.0	1.3	Dermal fibroblast IFN gamma	0.0	0.0
Dendritic cells LPS	0.0	0.0	Dermal fibroblast IL-4	0.0	0.0
Dendritic cells anti-CD40	0.0	0.0	IBD Colitis 2	0.0	0.5
Monocytes rest	0.0	49.3	IBD Crohn's	0.0	0.0
Monocytes LPS	0.0	79.0	Colon	0.0	15.1
Macrophages rest	0.0	9.0	Lung	0.0	100.0
Macrophages LPS	0.0	3.1	Thymus	0.0	95.3
HUVEC none	0.0	0.0	Kidney	0.0	32.3
HUVEC starved	0.0	0.0			

CNS_neurodegeneration_v1.0 Summary: Ag3339 This panel confirms the expression of the CG57488-01 gene at low levels in the brain in an independent group of individuals. Interestingly, this gene appears to be slightly upregulated in the temporal cortex of Alzheimer's disease patients. Therefore, therapeutic modulation of the activity of this gene or its protein product may be of use to decrease neuronal death in the treatment of Alzheimer's disease. Ag3254 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3254 Expression of the CG57488-01 gene is highest in lung cancer cell line SHP-77 (CT = 29.1). Expression of this gene is also higher in fetal lung (CT = 32.9) than in adult lung (CT = 37.7), suggesting that expression of this gene can be used to distinguish fetal lung from adult lung. In addition, significant expression of this gene is seen in adult and fetal kidney. This gene resembles members of the alpha-2-macroglobulin family. It has been shown that patients with chronic renal failure treated with haemodialysis have significantly lower blood serum levels of alpha-2-macroglobulin than healthy patients (ref. 1). Therefore, therapeutic modulation of the activity of this gene or its protein product, using small molecule drugs, antibodies, or protein therapeutics, may be used as a treatment for patients with renal failure.

Among tissues with metabolic or endocrine function, this gene is expressed at low levels in adrenal gland, heart, and pancreas. Therefore, therapeutic modulation of the activity of this gene or its protein product may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

The CG57488-01 gene is expressed at low levels in some regions of the CNS, including fetal brain, substantia nigra and spinal cord. Alpha-2-macroglobulin, a serum pan-protease inhibitor, has been implicated in Alzheimer's disease based on its ability to mediate the clearance and degradation of A-beta, the major component of amyloid beta deposits (ref.

2). Therefore, the CG57488-01 gene may also play a role in the development of Alzheimer's disease.

References:

1. Bartelik S, Starzyk J, Krajewska R. Concentration of prealbumin, ceruloplasmin, alpha-macroglobulin and haptoglobin in blood serum of patients with chronic non-A, non-B hepatitis treated with hemodialysis for chronic renal failure. *Wiad Lek* 1992 Oct;45(19-20):733-6

In 25 patients with chronic renal failure, treated with haemodialysis (13 patients with chronic non-A, non-B hepatitis, and 12 cases without evidence of hepatocellular damage), and in 20 healthy persons, blood serum concentrations were determined of prealbumin, ceruloplasmin, alpha 2-macroglobulin, and haptoglobin. It was found that the concentrations of these proteins in both subgroups of patients were not significantly different. The concentration of prealbumin was higher, and that of alpha 2-macroglobulin and haptoglobin was significantly lower in comparison with healthy subjects.

PMID: 1284260

2. Blacker D, Wilcox MA, Laird NM, Rodes L, Horvath SM, Go RC, Perry R, Watson B Jr, Bassett SS, McInnis MG, Albert MS, Hyman BT, Tanzi RE. Alpha-2 macroglobulin is genetically associated with Alzheimer disease. *Nat Genet* 1998 Aug;19(4):357-60

Alpha-2-macroglobulin (alpha-2M; encoded by the gene A2M) is a serum pan-protease inhibitor that has been implicated in Alzheimer disease (AD) based on its ability to mediate the clearance and degradation of A beta, the major component of beta-amyloid deposits. Analysis of a deletion in the A2M gene at the 5' splice site of 'exon II' of the bait region (exon 18) revealed that inheritance of the deletion (A2M-2) confers increased risk for AD (Mantel Haenzel odds ratio=3.56, P=0.001). The sibship disequilibrium test (SDT) also revealed a significant association between A2M and AD (P=0.00009). These values were comparable to those obtained for the APOE-epsilon4 allele in the same sample, but in contrast to APOE epsilon4, A2M-2 did not affect age of onset. The observed association of A2M with AD did not appear to account for the previously published linkage of AD to chromosome 12, which we were unable to confirm in this sample. A2M, LR(encoding the alpha-2M receptor) and the genes for two other LRP ligands, APOE and APP (encoding the amyloid beta protein precursor), have now all been genetically linked to AD, suggesting that these proteins may participate in a common neuropathogenic pathway leading to AD.

PMID: 9697696

AD 3 Temporal Ctx	26.8	Control 4 Occipital Ctx	51.8
AD 4 Temporal Ctx	0.0	Control (Path) 1 Occipital Ctx	100.0
AD 5 Inf Temporal Ctx	0.0	Control (Path) 2 Occipital Ctx	27.7
AD 5 Sup Temporal Ctx	0.0	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	0.0	Control (Path) 4 Occipital Ctx	0.0
AD 6 Sup Temporal Ctx	0.0	Control 1 Parietal Ctx	0.0
Control 1 Temporal Ctx	96.6	Control 2 Parietal Ctx	0.0
Control 2 Temporal Ctx	62.9	Control 3 Parietal Ctx	48.0
Control 3 Temporal Ctx	0.0	Control (Path) 1 Parietal Ctx	0.0
Control 3 Temporal Ctx	0.0	Control (Path) 2 Parietal Ctx	19.5
Control (Path) 1 Temporal Ctx	73.2	Control (Path) 3 Parietal Ctx	0.0
Control (Path) 2 Temporal Ctx	0.0	Control (Path) 4 Parietal Ctx	0.0

Table JC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3275, Run 215775538	Tissue Name	Rel. Exp.(%) Ag3275, Run 215775538
Adipose	0.0	Renal ca. TK-10	5.1
Melanoma* Hs688(A).T	0.0	Bladder	0.0
Melanoma* Hs688(B).T	5.5	Gastric ca. (liver met.) NCI-N87	9.4
Melanoma* M14	0.0	Gastric ca. KATO III	5.1
Melanoma* LOXIMVI	0.0	Colon ca. SW-948	3.7
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	0.0
Squamous cell carcinoma SCC-4	4.4	Colon ca.* (SW480 met) SW620	4.0
Testis Pool	0.0	Colon ca. HT29	4.2
Prostate ca.* (bone met) PC-3	0.0	Colon ca. HCT-116	0.0
Prostate Pool	0.0	Colon ca. CaCo-2	0.0
Placenta	0.0	Colon cancer tissue	0.0
Uterus Pool	0.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.0	Colon ca. Colo-205	0.0

Ovarian ca. SK-OV-3	0.0	Colon ca. SW-48	17.2
Ovarian ca. OVCAR-4	0.0	Colon Pool	3.2
Ovarian ca. OVCAR-5	0.0	Small Intestine Pool	0.0
Ovarian ca. IGROV-1	0.0	Stomach Pool	0.0
Ovarian ca. OVCAR-8	0.0	Bone Marrow Pool	0.0
Ovary	0.0	Fetal Heart	0.0
Breast ca. MCF-7	0.0	Heart Pool	10.4
Breast ca. MDA-MB-231	10.4	Lymph Node Pool	4.8
Breast ca. BT 549	0.0	Fetal Skeletal Muscle	0.0
Breast ca. T47D	0.0	Skeletal Muscle Pool	10.5
Breast ca. MDA-N	0.0	Spleen Pool	4.6
Breast Pool	0.0	Thymus Pool	5.0
Trachea	0.0	CNS cancer (glio/astro) U87-MG	5.0
Lung	0.0	CNS cancer (glio/astro) U-118-MG	0.0
Fetal Lung	0.0	CNS cancer (neuro;met) SK-N-AS	61.6
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	6.7	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	7.5	CNS cancer (glio) SNB-19	0.0
Lung ca. SHP-77	59.0	CNS cancer (glio) SF-295	0.0
Lung ca. A549	4.4	Brain (Amygdala) Pool	0.0
Lung ca. NCI-H526	10.2	Brain (cerebellum)	0.0
Lung ca. NCI-H23	100.0	Brain (fetal)	5.3
Lung ca. NCI-H460	7.6	Brain (Hippocampus) Pool	0.0
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	0.0
Lung ca. NCI-H522	5.6	Brain (Substantia nigra) Pool	1.3
Liver	0.0	Brain (Thalamus) Pool	0.0
Fetal Liver	0.0	Brain (whole)	0.0
Liver ca. HepG2	0.0	Spinal Cord Pool	0.0
Kidney Pool	0.0	Adrenal Gland	2.4
Fetal Kidney	55.5	Pituitary gland Pool	0.0
Renal ca. 786-0	0.0	Salivary Gland	0.0
Renal ca. A498	0.0	Thyroid (female)	0.0
Renal ca. ACHN	9.4	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.0	Pancreas Pool	0.0

Table JD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3275, Run 164634885	Tissue Name	Rel. Exp.(%) Ag3275, Run 164634885
Secondary Th1 act	0.7	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.8	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.5	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.6	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.7	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	1.3	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	4.5
LAK cells IL-2+IL-12	0.0	Lupus kidney	3.6
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	3.6
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	9.5
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	1.7
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	3.6
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0

Two Way MLR 5 day	0.3	HPAEC none	1.4
Two Way MLR 7 day	0.9	HPAEC TNF alpha + IL-1 beta	0.7
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	10.9
Macrophages rest	0.0	Lung	2.5
Macrophages LPS	0.0	Thymus	100.0
HUVEC none	0.0	Kidney	1.4
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag3275 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3275 Expression of the CG57526-01 gene is highest in lung cancer cell line NCI-H23 (CT=32.8). Expression of this gene is higher in several additional lung cancer cell lines when compared to normal lung. Thus, expression of this gene may be used as a marker for lung cancer. Furthermore, therapeutic modulation of the activity of this gene or its protein product, using small molecule drugs, antibodies or protein therapeutics, may be of use in the treatment of lung cancer. The CG57526-01 gene encodes a protein with homology to sodium- and chloride-dependent transporter XT3, a protein that mediates transit of structurally related small hydrophilic substances across plasma membranes (ref. 1).

Interestingly, while there is low expression of this gene in fetal kidney (CT=33.6), this gene does not seem to be expressed at detectable levels in adult kidney. This observation

suggests that expression of this gene can be used to distinguish fetal from adult kidney. Expression of this gene is consistent with what is known about the XT3 transporter (ref. 1).

References:

1. Nash SR, Giros B, Kingsmore SF, Kim KM, el-Mestikawy S, Dong Q, Fumagalli F, Seldin MF, Caron MG. Cloning, gene structure and genomic localization of an orphan transporter from mouse kidney with six alternatively-spliced isoforms. *Receptors Channels* 1998;6(2):113-28

Two genes were identified and characterized that express cDNAs related to previously identified neurotransmitter and/or osmolyte transporters, but which are expressed specifically in the kidney. RNA transcribed from one of these two genes (XT2) was found to undergo an extensive degree of alternative splicing to generate six distinct isoforms. The intron-exon structure of the XT2 gene and the sites of alternative splicing were identified. Expression of the second gene (XT3) was found to be conserved in human kidney, and partial sequence was obtained from a human cDNA library. The expressions of both XT2 and XT3 RNAs were determined in mouse and human tissues, respectively, and the locations of the two genes within the mouse genome were identified. Screening experiments to identify the substrate(s) of these proteins failed to identify specific uptake with any of the tested compounds; however, immunofluorescent microscopy demonstrated that epitope-tagged variants of the protein products of the XT2 and XT3 cDNAs were present on the plasma membrane of transfected cells.

PMID: 9932288

Panel 4D Summary: Ag3275 Expression of the CG57526-01 gene is highest in thymus (CT = 29). Therefore, expression of this gene may be used to distinguish thymus from the other samples on this panel. In addition, the putative ion transporter encoded for by the CG57526-01 gene could play an important role in T cell development. Small molecule therapeutics or antibody therapeutics designed against the protein encoded for by this gene could be utilized to modulate immune function (T cell development) and be important for organ transplant, AIDS treatment or post chemotherapy immune reconstitution. In addition, this gene is expressed at low levels in the NCI-H292 mucoepidermoid cell line, consistent with its expression in lung cancer cell lines on General_screening_panel_v1.4.

NOV13

Expression of NOV13/CG57570-01 was assessed using the primer-probe set Ag3288, described in Table KA. Results of the RTQ-PCR runs are shown in Tables KB, KC and KD.

Table KA. Probe Name Ag3288

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-tctacaccatcagctgtatga-3'	22	1380	288
Probe	TET-5'-caccacctcacactcatcttcatca-3'-TAMRA	26	1411	289
Reverse	5'-gcagtcgagctgtcatatagaa-3'	22	1439	290

Table KB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3288, Run 210058660	Rel. Exp.(%) Ag3288, Run 229929907	Tissue Name	Rel. Exp.(%) Ag3288, Run 210058660	Rel. Exp.(%) Ag3288, Run 229929907
AD 1 Hippo	26.6	31.0	Control (Path) 3 Temporal Ctx	13.3	15.1
AD 2 Hippo	43.5	48.0	Control (Path) 4 Temporal Ctx	33.7	36.3
AD 3 Hippo	15.0	14.8	AD 1 Occipital Ctx	25.7	15.5
AD 4 Hippo	13.0	11.5	AD 2 Occipital Ctx (Missing)	0.0	0.0
AD 5 hippo	97.3	100.0	AD 3 Occipital Ctx	16.5	15.8
AD 6 Hippo	100.0	90.1	AD 4 Occipital Ctx	26.1	35.1
Control 2 Hippo	29.3	28.9	AD 5 Occipital Ctx	26.4	28.5
Control 4 Hippo	33.7	41.2	AD 6 Occipital Ctx	33.2	37.6
Control (Path) 3 Hippo	22.8	27.9	Control 1 Occipital Ctx	8.8	10.4
AD 1 Temporal Ctx	34.2	35.8	Control 2 Occipital Ctx	51.8	59.9
AD 2 Temporal Ctx	47.3	52.1	Control 3 Occipital Ctx	28.5	12.8
AD 3 Temporal Ctx	14.0	18.6	Control 4 Occipital Ctx	16.5	17.8
AD 4 Temporal Ctx	34.6	46.7	Control (Path) 1 Occipital Ctx	66.0	82.4
AD 5 Inf Temporal Ctx	80.1	100.0	Control (Path) 2 Occipital Ctx	11.3	14.4
AD 5 SupTemporal Ctx	64.2	85.9	Control (Path) 3 Occipital Ctx	9.5	8.5
AD 6 Inf Temporal Ctx	68.8	87.1	Control (Path) 4 Occipital Ctx	13.9	17.7
AD 6 Sup Temporal Ctx	66.4	87.1	Control 1 Parietal Ctx	11.1	15.8
Control 1 Temporal Ctx	11.3	16.2	Control 2 Parietal Ctx	48.0	66.0
Control 2 Temporal Ctx	33.0	36.3	Control 3 Parietal Ctx	17.0	22.2
Control 3 Temporal Ctx	19.2	18.9	Control (Path) 1 Parietal Ctx	55.5	66.4
Control 4 Temporal Ctx	14.7	17.8	Control (Path) 2 Parietal Ctx	30.6	34.2
Control (Path) 1 Temporal Ctx	32.3	50.7	Control (Path) 3 Parietal Ctx	14.3	11.3

Control (Path) 2 Temporal Ctx	36.9	13.2	Control (Path) 4 Parietal Ctx	37.1	43.2
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Table KC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3288, Run 216516909	Tissue Name	Rel. Exp.(%) Ag3288, Run 216516909
Adipose	15.8	Renal ca. TK-10	24.0
Melanoma* Hs688(A).T	38.4	Bladder	26.8
Melanoma* Hs688(B).T	51.4	Gastric ca. (liver met.) NCI- N87	55.1
Melanoma* M14	43.5	Gastric ca. KATO III	53.6
Melanoma* LOXIMVI	25.0	Colon ca. SW-948	19.1
Melanoma* SK-MEL-5	52.9	Colon ca. SW480	41.2
Squamous cell carcinoma SCC-4	16.5	Colon ca.* (SW480 met) SW620	14.4
Testis Pool	44.4	Colon ca. HT29	9.5
Prostate ca.* (bone met) PC-3	57.4	Colon ca. HCT-116	50.7
Prostate Pool	16.2	Colon ca. CaCo-2	9.5
Placenta	4.3	Colon cancer tissue	7.3
Uterus Pool	4.9	Colon ca. SW1116	6.7
Ovarian ca. OVCAR-3	37.9	Colon ca. Colo-205	10.5
Ovarian ca. SK-OV-3	39.0	Colon ca. SW-48	7.3
Ovarian ca. OVCAR-4	18.0	Colon Pool	15.9
Ovarian ca. OVCAR-5	63.3	Small Intestine Pool	15.0
Ovarian ca. IGROV-1	14.5	Stomach Pool	9.6
Ovarian ca. OVCAR-8	12.1	Bone Marrow Pool	9.4
Ovary	17.2	Fetal Heart	72.7
Breast ca. MCF-7	32.5	Heart Pool	66.9
Breast ca. MDA-MB-231	47.3	Lymph Node Pool	19.3
Breast ca. BT 549	58.2	Fetal Skeletal Muscle	17.6
Breast ca. T47D	73.7	Skeletal Muscle Pool	63.7
Breast ca. MDA-N	12.6	Spleen Pool	11.0
Breast Pool	14.6	Thymus Pool	7.5
Trachea	14.6	CNS cancer (glio/astro) U87- MG	30.8
Lung	7.5	CNS cancer (glio/astro) U- 118-MG	44.1
Fetal Lung	63.7	CNS cancer (neuro;met) SK- N-AS	37.9
Lung ca. NCI-N417	2.7	CNS cancer (astro) SF-539	33.2
Lung ca. LX-1	19.5	CNS cancer (astro) SNB-75	34.6
Lung ca. NCI-H146	4.9	CNS cancer (glio) SNB-19	18.9
Lung ca. SHP-77	12.0	CNS cancer (glio) SF-295	64.2
Lung ca. A549	24.8	Brain (Amygdala) Pool	13.4
Lung ca. NCI-H526	8.8	Brain (cerebellum)	100.0
Lung ca. NCI-H23	23.8	Brain (fetal)	28.5
Lung ca. NCI-H460	29.5	Brain (Hippocampus) Pool	21.5
Lung ca. HOP-62	23.0	Cerebral Cortex Pool	22.8
Lung ca. NCI-H522	36.1	Brain (Substantia nigra) Pool	19.2
Liver	0.5	Brain (Thalamus) Pool	26.8
Fetal Liver	27.2	Brain (whole)	40.9
Liver ca. HepG2	0.2	Spinal Cord Pool	19.8
Kidney Pool	23.0	Adrenal Gland	40.3
Fetal Kidney	21.2	Pituitary gland Pool	5.8

Renal ca. 786-0	32.1	Salivary Gland	6.4
Renal ca. A498	17.6	Thyroid (female)	17.2
Renal ca. ACHN	36.1	Pancreatic ca. CAPAN2	14.8
Renal ca. UO-31	21.0	Pancreas Pool	22.8

Table KD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3288, Run 165007638	Tissue Name	Rel. Exp.(%) Ag3288, Run 165007638
Secondary Th1 act	15.0	HUVEC IL-1beta	10.7
Secondary Th2 act	15.8	HUVEC IFN gamma	9.3
Secondary Tr1 act	15.0	HUVEC TNF alpha + IFN gamma	20.9
Secondary Th1 rest	3.0	HUVEC TNF alpha + IL4	14.9
Secondary Th2 rest	8.5	HUVEC IL-11	6.6
Secondary Tr1 rest	4.4	Lung Microvascular EC none	9.3
Primary Th1 act	28.5	Lung Microvascular EC TNFalpha + IL-1beta	58.2
Primary Th2 act	19.5	Microvascular Dermal EC none	22.4
Primary Tr1 act	24.0	Microvascular Dermal EC TNFalpha + IL-1beta	63.3
Primary Th1 rest	11.5	Bronchial epithelium TNFalpha + IL1beta	20.6
Primary Th2 rest	8.5	Small airway epithelium none	3.8
Primary Tr1 rest	4.6	Small airway epithelium TNFalpha + IL-1beta	48.6
CD45RA CD4 lymphocyte act	12.2	Coronary artery SMC rest	11.7
CD45RO CD4 lymphocyte act	21.2	Coronary artery SMC TNFalpha + IL-1beta	9.1
CD8 lymphocyte act	14.2	Astrocytes rest	16.4
Secondary CD8 lymphocyte rest	22.1	Astrocytes TNFalpha + IL-1beta	12.9
Secondary CD8 lymphocyte act	10.8	KU-812 (Basophil) rest	16.8
CD4 lymphocyte none	5.1	KU-812 (Basophil) PMA/ionomycin	50.3
2ry Th1/Th2/Tr1_anti-CD95 CH11	4.0	CCD1106 (Keratinocytes) none	14.0
LAK cells rest	4.8	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	10.8
LAK cells IL-2	10.6	Liver cirrhosis	3.3
LAK cells IL-2+IL-12	15.7	Lupus kidney	1.6
LAK cells IL-2+IFN gamma	19.3	NCI-H292 none	14.6
LAK cells IL-2+ IL-18	14.2	NCI-H292 IL-4	18.9
LAK cells PMA/ionomycin	5.7	NCI-H292 IL-9	16.3
NK Cells IL-2 rest	7.9	NCI-H292 IL-13	13.1
Two Way MLR 3 day	11.5	NCI-H292 IFN gamma	11.2
Two Way MLR 5 day	9.7	HPAEC none	11.5
Two Way MLR 7 day	6.7	HPAEC TNF alpha + IL-1 beta	31.0
PBMC rest	3.6	Lung fibroblast none	13.9
PBMC PWM	61.6	Lung fibroblast TNF alpha + IL-1 beta	13.6
PBMC PHA-L	31.6	Lung fibroblast IL-4	28.1
Ramos (B cell) none	13.7	Lung fibroblast IL-9	22.2
Ramos (B cell) ionomycin	94.6	Lung fibroblast IL-13	13.5
B lymphocytes PWM	63.7	Lung fibroblast IFN gamma	23.7
B lymphocytes CD40L and	100.0	Dermal fibroblast CCD1070 rest	30.4

studies on the involvement of LfR, MTF and DCT1 in iron uptake by and CP in iron egress from different types of brain cells as well as control mechanisms of expression of these proteins in the brain are critical for elucidating the causes of excessive accumulation of iron in the brain and neuronal death in neurodegenerative diseases.

5 PMID: 9729418

General_screening_panel_v1.4 Summary: Ag3288 The CG57570-01 gene is expressed at high to moderate levels across almost all samples in this panel, with highest expression in the cerebellum (CT=26.7). This gene is also moderately expressed in all other regions of the CNS examined, including in amygdala, substantia nigra, thalamus, cerebral
10 cortex, and spinal cord, suggesting that this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

This gene is also expressed in a number of tissues with metabolic or endocrine function, including adipose, adrenal gland, gastrointestinal tract, pancreas, skeletal muscle and
15 thyroid. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes. Interestingly, this gene is differentially expressed in adult liver (CT = 34) vs fetal liver (CT = 29), suggesting that expression of this gene may be used to distinguish adult and fetal liver.

In addition, there is substantial expression of this gene associated with cancer cell
20 lines. Therefore, therapeutic modulation of the activity of this gene or its protein product, through the use of small molecule drugs, protein therapeutics or antibodies, might be beneficial in the treatment of cancer.

Panel 4D Summary: Ag3288 The CG57570-01 gene is expressed at high to moderate levels in a wide range of cell types of significance in the immune response in health and
25 disease, with the highest expression being detected in activated B cells (CT = 25). Therefore, targeting the CG57570-01 gene product with a small molecule drug or antibody therapeutic may modulate the functions of cells of the immune system, and particularly B cells, and lead to improvement of the symptoms of patients suffering from rheumatoid diseases, B hyperglobulinemia and autoimmune disorders.

30 **NOV14**

Expression of gene CG57593-01 was assessed using the primer-probe set Ag3292, described in Table LA.

Table LA. Probe Name Ag3292

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-tggtcatacatcaatccaat-3'	22	957	291
Probe	TET-5'-tggtcatgtgtgatattcacactct-3'-TAMRA	26	991	292
Reverse	5'-gaaagccaacaccaagaaag-3'	21	1031	293

CNS_neurodegeneration_v1.0 Summary: Ag3292 Expression of the CG57593-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3292 Expression of the CG57593-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag3292 Expression of the CG57593-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV15

Expression of NOV15/CG57652-01 was assessed using the primer-probe sets Ag1762 and Ag1763, described in Tables MA and MB. Results of the RTQ-PCR runs are shown in Tables MC and MD.

Table MA. Probe Name Ag1762

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-caaacagggactgagctgtaac-3'	22	766	295
Probe	TET-5'-tacactgttcacgaccagtgtgccat-3'-TAMRA	26	797	296
Reverse	5'-gcataggtgtctgacttcacaa-3'	21	835	297

Table MB. Probe Name Ag1763

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ggtgctctggaagtccagtat-3'	22	1255	298
Probe	TET-5'-accctcgacagggtgtcaacctccta-3'-TAMRA	26	1284	299
Reverse	5'-cttgaataatcgagccctatc-3'	22	1324	300

Table MC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1762, Run 157720756	Rel. Exp.(%) Ag1763, Run 157717718	Tissue Name	Rel. Exp.(%) Ag1762, Run 157720756	Rel. Exp.(%) Ag1763, Run 157717718
Liver adenocarcinoma	26.6	25.7	Kidney (fetal)	2.5	3.7
Pancreas	1.6	2.8	Renal ca. 786-0	0.2	0.1
Pancreatic ca. CAPAN 2	9.2	8.1	Renal ca. A498	20.3	18.7
Adrenal gland	6.7	6.2	Renal ca. RXF 393	0.7	0.6
Thyroid	5.0	3.4	Renal ca. ACHN	4.7	4.4
Salivary gland	13.6	23.7	Renal ca. UO-31	21.9	15.8
Pituitary gland	3.9	3.9	Renal ca. TK-10	1.7	2.2
Brain (fetal)	1.7	3.6	Liver	1.1	1.0
Brain (whole)	6.6	8.2	Liver (fetal)	3.7	3.5
Brain (amygdala)	6.5	8.2	Liver ca. (hepatoblast) HepG2	2.4	1.3

Brain (cerebellum)	2.1	3.4	Lung	15.9	16.7
Brain (hippocampus)	28.9	35.6	Lung (fetal)	7.7	12.6
Brain (substantia nigra)	0.8	1.3	Lung ca. (small cell) LX-1	3.5	1.6
Brain (thalamus)	1.9	2.4	Lung ca. (small cell) NCI-H69	2.4	2.3
Cerebral Cortex	25.5	18.3	Lung ca. (s.cell var.) SHP-77	3.9	4.1
Spinal cord	2.2	3.3	Lung ca. (large cell)NCI-H460	0.9	1.1
glio/astro U87-MG	4.9	5.6	Lung ca. (non-sm. cell) A549	5.0	3.5
glio/astro U-118-MG	46.7	38.2	Lung ca. (non-s.cell) NCI-H23	1.3	2.3
astrocytoma SW1783	7.3	3.8	Lung ca. (non-s.cell) HOP-62	1.5	2.4
neuro*; met SK-N-AS	24.1	25.7	Lung ca. (non-s.cl) NCI-H522	3.0	2.9
astrocytoma SF-539	4.8	5.8	Lung ca. (squam.) SW 900	7.4	7.9
astrocytoma SNB-75	15.1	10.0	Lung ca. (squam.) NCI-H596	0.2	0.3
glioma SNB-19	1.5	2.1	Mammary gland	7.9	9.2
glioma U251	3.0	1.6	Breast ca.* (pl.ef) MCF-7	16.5	1.2
glioma SF-295	5.1	5.8	Breast ca.* (pl.ef) MDA-MB-231	8.6	8.1
Heart (fetal)	3.2	1.4	Breast ca.* (pl.ef) T47D	5.4	5.6
Heart	1.3	0.9	Breast ca. BT-549	6.5	5.9
Skeletal muscle (fetal)	6.7	5.8	Breast ca. MDA-N	2.4	1.2
Skeletal muscle	0.8	0.3	Ovary	13.2	10.8
Bone marrow	15.0	14.7	Ovarian ca. OVCAR-3	1.6	1.3
Thymus	100.0	100.0	Ovarian ca. OVCAR-4	2.0	0.9
Spleen	24.5	39.0	Ovarian ca. OVCAR-5	3.9	3.9
Lymph node	26.6	40.1	Ovarian ca. OVCAR-8	11.8	9.2
Colorectal	7.5	8.7	Ovarian ca. IGROV-1	1.5	2.7
Stomach	7.5	13.8	Ovarian ca.* (ascites) SK-OV-3	8.9	6.0
Small intestine	19.8	19.5	Uterus	5.5	8.2
Colon ca. SW480	5.1	6.1	Placenta	14.2	12.9
Colon ca.* SW620(SW480 met)	0.9	1.2	Prostate	7.6	10.7
Colon ca. HT29	1.3	0.7	Prostate ca.* (bone met)PC-3	10.7	11.1
Colon ca. HCT-116	5.4	3.2	Testis	9.0	10.7
Colon ca. CaCo-2	3.8	3.2	Melanoma Hs688(A).T	5.9	4.4
Colon ca. tissue(ODO3866)	26.1	19.5	Melanoma* (met) Hs688(B).T	4.7	2.6
Colon ca. HCC-2998	8.1	4.3	Melanoma UACC-62	0.3	0.4
Gastric ca.* (liver met) NCI-N87	21.6	21.0	Melanoma M14	0.1	0.0

Bladder	3.7	2.0	Melanoma LOX IMVI	2.2	0.7
Trachea	46.7	50.3	Melanoma* (met) SK-MEL-5	0.4	0.3
Kidney	0.2	0.7	Adipose	2.6	2.5

Table MD. Panel 5 Islet

Tissue Name	Rel. Exp.(%) Ag1763, Run 242285275	Tissue Name	Rel. Exp.(%) Ag1763, Run 242285275
97457_Patient-02go_adipose	22.2	94709_Donor 2 AM - A_adipose	55.9
97476_Patient-07sk_skeletal muscle	7.5	94710_Donor 2 AM - B_adipose	11.0
97477_Patient-07ut_uterus	13.8	94711_Donor 2 AM - C_adipose	16.0
97478_Patient-07pl_placenta	34.2	94712_Donor 2 AD - A_adipose	68.8
99167_Bayer Patient 1	47.3	94713_Donor 2 AD - B_adipose	56.6
97482_Patient-08ut_uterus	12.0	94714_Donor 2 AD - C_adipose	59.5
97483_Patient-08pl_placenta	29.5	94742_Donor 3 U - A_Mesenchymal Stem Cells	33.2
97486_Patient-09sk_skeletal muscle	1.9	94743_Donor 3 U - B_Mesenchymal Stem Cells	26.4
97487_Patient-09ut_uterus	21.5	94730_Donor 3 AM - A_adipose	73.7
97488_Patient-09pl_placenta	23.8	94731_Donor 3 AM - B_adipose	26.1
97492_Patient-10ut_uterus	23.7	94732_Donor 3 AM - C_adipose	26.4
97493_Patient-10pl_placenta	65.1	94733_Donor 3 AD - A_adipose	55.5
97495_Patient-11go_adipose	23.3	94734_Donor 3 AD - B_adipose	31.0
97496_Patient-11sk_skeletal muscle	4.4	94735_Donor 3 AD - C_adipose	41.5
97497_Patient-11ut_uterus	12.9	77138_Liver_HepG2untreated	35.6
97498_Patient-11pl_placenta	15.1	73556_Heart_Cardiac stromal cells (primary)	44.8
97500_Patient-12go_adipose	18.2	81735_Small Intestine	74.7
97501_Patient-12sk_skeletal muscle	9.2	72409_Kidney_Proximal Convoluted Tubule	6.4
97502_Patient-12ut_uterus	18.9	82685_Small intestine_Duodenum	22.7
97503_Patient-12pl_placenta	18.7	90650_Adrenal_Adrenocortical adenoma	11.3
94721_Donor 2 U - A_Mesenchymal Stem Cells	28.3	72410_Kidney_HRCE	100.0
94722_Donor 2 U - B_Mesenchymal Stem Cells	22.8	72411_Kidney_HRE	62.0
94723_Donor 2 U - C_Mesenchymal Stem Cells	37.1	73139_Uterus_Uterine smooth muscle cells	16.4

Panel 1.3D Summary: Ag1762/Ag1763 Results from experiments using two different probe/primer sets are in excellent agreement. In both experiments, the CG57652-01 gene is expressed at highest levels in thymus tissue (CT = 27.3/25.8).

5

In addition, this gene is expressed at moderate levels in all regions of the central nervous system examined, including amygdala, hippocampus, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

This gene is expressed in a number of tissues with metabolic or endocrine function, including adipose, adrenal gland, gastrointestinal tract, pancreas, skeletal muscle and thyroid. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes. The CG57652-01 gene encodes a variant of the diacylglycerol kinase- α gene (ref. 1). It has been shown that unsaturated fatty acids can lead to increased protein kinase C (PKC) activation by a deactivation of diacylglycerol kinase- α (ref. 2-3). Therefore, therapeutic modulation of the activity of the CG57652-01 gene or its protein product using small molecule drugs may be used to combat the negative effects of increased fatty acids in patients with diabetes.

References:

1. Schaap D, de Widt J, van der Wal J, Vandekerckhove J, van Damme J, Gussow D, Ploegh HL, van Blitterswijk WJ, van der Bend RL. Purification, cDNA-cloning and expression of human diacylglycerol kinase. *FEBS Lett* 1990 Nov 26;275(1-2):151-8

Diacylglycerol (DG) kinase attenuates the level of the second messenger DG in signal transduction, and therefore possibly modulates protein kinase C (PKC). DG kinase was purified to homogeneity from human white blood cells, showing an Mr of 86 kDa as determined by SDS-PAGE and gel filtration. Two amino acid sequences of tryptic peptides from DG kinase were determined and degenerate oligonucleotides were prepared and used in the polymerase chain reaction. An amplified DNA fragment was subsequently used to clone the full-length human DG kinase cDNA. This sequence is the human homolog of a porcine DG kinase cDNA sequence reported recently. The sequence contains a double EF-hand structure typical for Ca^{2+} binding proteins. DG kinase further contains a double cysteine repeat that is present in all PKC isoforms, where it constitutes the phorbol ester (and most likely diacylglycerol) binding site. Therefore we speculate that the double cysteine repeat in DG kinase is involved in DG binding. DG kinase is transcribed as a single mRNA of 3.2 kb, that is highly expressed in T-lymphocytes. The human DG kinase cDNA when transfected in mammalian cells (COS-7) results in a 6-7-fold increase of DG kinase activity.

PMID: 2175712

2. Du X, Jiang Y, Qian W, Lu X, Walsh JP. Fatty acids inhibit growth-factor-induced diacylglycerol kinase α activation in vascular smooth-muscle cells. *Biochem J* 2001 Jul 1;357(Pt 1):275-82.

We have previously shown that unsaturated fatty acids amplify platelet-derived-growth-factor (PDGF)-induced protein kinase C (PKC) activation in vascular smooth-muscle cells (VSMCs). Diacylglycerol-induced PKC activation is normally terminated by diacylglycerol kinases (DGKs). We thus hypothesized that fatty acids act by inhibiting a DGK.

5 Fractionation of VSMC extracts demonstrated that the DGK alpha isoform was the major DGK activity present. PDGF markedly increased the DGK activity of cultured cells. An inhibitor selective for the DGK alpha isoform, R59949 [3-[2-[4-(bis-(4-fluorophenyl)methylene]piperidin-1-yl)ethyl]-2,3-dihydro-2-thioxo-4(1H)-quinazolinone], abolished the growth-factor-induced increase in DGK activity, but had little effect on basal
10 activity. PDGF thus selectively activates DGKalpha. Epidermal growth factor and alpha-thrombin stimulated total DGK activity similarly to PDGF. Activation by epidermal growth factor was sensitive to R59949, again suggesting involvement of DGKalpha. However, the alpha-thrombin-induced activity was unaffected by this agent. Unsaturated fatty acids inhibited growth-factor-induced DGKalpha activation, but had no effect on basal activity.
15 Fatty acids also amplified the PDGF-induced increase in cell diacylglycerol content. These results indicate that inhibition of DGKalpha contributes to fatty-acid-induced amplification of PKC activation. Increased levels of fatty acids in diabetes may thus contribute to chronic PKC activation associated with this disorder.

PMID: 11415460

20 3. Koya D, Lee IK, Ishii H, Kanoh H, King GL. Prevention of glomerular dysfunction in diabetic rats by treatment with d-alpha-tocopherol. J Am Soc Nephrol 1997 Mar;8(3):426-35.

Because d-alpha-tocopherol (vitamin E) has been shown to decrease diacylglycerol (DAG) levels and prevent the activation of protein kinase C (PKC), which is associated with
25 retinal and renal dysfunctions in diabetes, the study presented here characterized the effect of d-alpha-tocopherol treatment to prevent glomerular hyperfiltration and increased albuminuria as well as PKC activities in streptozotocin (STZ)-induced diabetic rats. Two weeks after the induction of diabetes, total DAG content and PKC activity in glomeruli were significantly increased in diabetic rats by 106.4 +/- 16.8% and 66.4 +/- 8.4%, respectively, compared with
30 control rats. Intraperitoneal injection of d-alpha-tocopherol (40 mg/kg of body weight) every other day prevented the increases in total DAG content and PKC activity in glomeruli of diabetic rats. Glomerular filtration rate (GFR) and filtration fraction (FF) were significantly elevated to 4.98 +/- 0.34 mL/min and 0.36 +/- 0.05, respectively, in diabetic rats, compared with 2.90 +/- 0.14 mL/min and 0.25 +/- 0.02, respectively, in control rats. These hemodynamic

abnormalities in diabetic rats were normalized to 2.98 ± 0.09 mL/min and 0.24 ± 0.01 , respectively, by d-alpha-tocopherol. Albuminuria in 10-wk diabetic rats was significantly increased to 9.1 ± 2.2 mg/day compared with 1.2 ± 0.3 mg/day in control rats, whereas d-alpha-tocopherol treatment improved albumin excretion rate to 2.4 ± 0.6 mg/day in diabetic rats. To clarify the mechanism of d-alpha-tocopherol's effect on DAG-PKC pathway, the activity and protein levels of DAG kinase alpha and gamma, which metabolize DAG to phosphatidic acid, were examined. Treatment with d-alpha-tocopherol increased DAG kinase activity in the glomeruli of both control and diabetic rats, by $22.6 \pm 3.6\%$ and $28.5 \pm 2.3\%$ respectively, although no differences were observed in the basal DAG kinase activity between control and diabetic rats. Because immunoblotting studies did not exhibit any difference in the protein levels of DAG kinase alpha and gamma, the effect of d-alpha-tocopherol is probably modulating the enzyme kinetics of DAG kinase. These findings suggest that the increases in DAG-PKC pathway play an important role for the development of glomerular hyperfiltration and increased albuminuria in diabetes and that d-alpha-tocopherol treatment could be preventing early changes of diabetic renal dysfunctions by normalizing the increases in DAG and PKC levels in glomerular cells.

PMID: 9071711

Panel 5 Islet Summary: Ag1763 The CG57652-01 gene is expressed at low levels in the majority of samples on this panel. This gene has a low level of expression in the islets of Langerhans (patient 1). Diacylglycerol kinase attenuates protein kinase C activation, which may in turn, reduce insulin secretion (ref. 1). Since the secretion of insulin is enhanced by activation of protein kinase C, an inhibitor of diacylglycerol kinase encoded by the CG57652-01 gene may be a treatment for the insulin secretory defect in Type 2 diabetes.

References:

1. Formisano P, Beguinot F. The role of protein kinase C isoforms in insulin action. J Endocrinol Invest. 2001 Jun;24(6):460-7.

Insulin action on target tissues is mediated by specific tyrosine kinase receptors. Upon ligand binding insulin receptors autophosphorylate and phosphorylate intracellular substrates on tyrosine residues. These early events of insulin action are followed by the activation of a number of enzymes, including protein kinase C (PKC). At least 14 PKC isoforms have been identified and cloned to date. PKCs appear to play dual roles in insulin signaling. For instance, they are involved in transduction of specific insulin signals but also contribute to the generation of insulin resistance. In this article, we will analyze the experimental evidence

addressing the mechanism by which insulin might activate individual PKC isoforms as well as the role of single PKCs in insulin-induced bioeffects.

PMID: 11434672

NOV16

- 5 Expression of NOV16/CG57562-01 was assessed using the primer-probe sets Ag3287 and Ag1179, described in Tables NA and NB. Results of the RTQ-PCR runs are shown in Tables NC, ND, NE and NF.

Table NA. Probe Name Ag3287

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-cgctacagatgttcaagatcct-3'	22	3018	301
Probe	TET-5'-ctacagccagagcgtcctctacctgg-3'-TAMRA	26	3064	302
Reverse	5'-cctggaagtcaactgaacttgac-3'	22	3095	303

Table NB. Probe Name Ag1179

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-cgctacagatgttcaagatcct-3'	22	3018	304
Probe	TET-5'-ctacagccagagcgtcctctacctgg-3'-TAMRA	26	3064	305
Reverse	5'-cctggaagtcaactgaacttgac-3'	22	3095	306

10 Table NC. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3287, Run 210058659	Tissue Name	Rel. Exp.(%) Ag3287, Run 210058659
AD 1 Hippo	23.2	Control (Path) 3 Temporal Ctx	6.8
AD 2 Hippo	35.6	Control (Path) 4 Temporal Ctx	42.0
AD 3 Hippo	11.8	AD 1 Occipital Ctx	19.9
AD 4 Hippo	11.9	AD 2 Occipital Ctx (Missing)	1.6
AD 5 Hippo	100.0	AD 3 Occipital Ctx	10.2
AD 6 Hippo	72.2	AD 4 Occipital Ctx	20.4
Control 2 Hippo	33.7	AD 5 Occipital Ctx	42.6
Control 4 Hippo	15.9	AD 6 Occipital Ctx	14.9
Control (Path) 3 Hippo	9.1	Control 1 Occipital Ctx	5.0
AD 1 Temporal Ctx	34.2	Control 2 Occipital Ctx	60.3
AD 2 Temporal Ctx	37.9	Control 3 Occipital Ctx	22.4
AD 3 Temporal Ctx	10.2	Control 4 Occipital Ctx	6.7
AD 4 Temporal Ctx	26.4	Control (Path) 1 Occipital Ctx	86.5
AD 5 Inf Temporal Ctx	88.9	Control (Path) 2 Occipital Ctx	12.5
AD 5 Sup Temporal Ctx	64.6	Control (Path) 3 Occipital Ctx	3.5
AD 6 Inf Temporal Ctx	53.2	Control (Path) 4 Occipital Ctx	26.2
AD 6 Sup Temporal Ctx	62.0	Control 1 Parietal Ctx	10.4
Control 1 Temporal Ctx	8.2	Control 2 Parietal Ctx	52.5
Control 2 Temporal Ctx	39.8	Control 3 Parietal Ctx	21.9

Control 3 Temporal Ctx	17.6	Control (Path) 1 Parietal Ctx	62.4
Control 3 Temporal Ctx	6.3	Control (Path) 2 Parietal Ctx	24.1
Control (Path) 1 Temporal Ctx	54.0	Control (Path) 3 Parietal Ctx	6.5
Control (Path) 2 Temporal Ctx	41.2	Control (Path) 4 Parietal Ctx	32.5

Table ND. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3287, Run 216516908	Tissue Name	Rel. Exp.(%) Ag3287, Run 216516908
Adipose	4.8	Renal ca. TK-10	26.4
Melanoma* Hs688(A).T	23.0	Bladder	19.9
Melanoma* Hs688(B).T	27.9	Gastric ca. (liver met.) NCI-N87	44.4
Melanoma* M14	31.6	Gastric ca. KATO III	39.8
Melanoma* LOXIMVI	33.7	Colon ca. SW-948	24.3
Melanoma* SK-MEL-5	31.0	Colon ca. SW480	39.8
Squamous cell carcinoma SCC-4	18.4	Colon ca.* (SW480 met) SW620	33.0
Testis Pool	12.2	Colon ca. HT29	10.0
Prostate ca. * (bone met) PC-3	49.7	Colon ca. HCT-116	48.3
Prostate Pool	6.8	Colon ca. CaCo-2	46.7
Placenta	23.0	Colon cancer tissue	19.1
Uterus Pool	4.5	Colon ca. SW1116	11.7
Ovarian ca. OVCAR-3	22.7	Colon ca. Colo-205	15.9
Ovarian ca. SK-OV-3	48.0	Colon ca. SW-48	10.9
Ovarian ca. OVCAR-4	20.6	Colon Pool	16.5
Ovarian ca. OVCAR-5	38.4	Small Intestine Pool	14.5
Ovarian ca. IGROV-1	34.2	Stomach Pool	9.2
Ovarian ca. OVCAR-8	13.5	Bone Marrow Pool	6.8
Ovary	11.7	Fetal Heart	18.0
Breast ca. MCF-7	33.0	Heart Pool	5.2
Breast ca. MDA-MB-231	49.3	Lymph Node Pool	19.8
Breast ca. BT 549	100.0	Fetal Skeletal Muscle	10.5
Breast ca. T47D	76.8	Skeletal Muscle Pool	5.8
Breast ca. MDA-N	24.0	Spleen Pool	12.0
Breast Pool	18.4	Thymus Pool	19.1
Trachea	16.6	CNS cancer (glio/astro) U87-MG	36.1
Lung	5.5	CNS cancer (glio/astro) U-118-MG	65.5
Fetal Lung	42.6	CNS cancer (neuro;met) SK-N-AS	69.3
Lung ca. NCI-N417	18.3	CNS cancer (astro) SF-539	22.4
Lung ca. LX-1	26.1	CNS cancer (astro) SNB-75	49.0
Lung ca. NCI-H146	17.8	CNS cancer (glio) SNB-19	31.9
Lung ca. SHP-77	37.9	CNS cancer (glio) SF-295	84.7
Lung ca. A549	24.1	Brain (Amygdala) Pool	7.5
Lung ca. NCI-H526	7.3	Brain (cerebellum)	42.3
Lung ca. NCI-H23	41.8	Brain (fetal)	26.8
Lung ca. NCI-H460	34.6	Brain (Hippocampus) Pool	8.2
Lung ca. HOP-62	13.4	Cerebral Cortex Pool	9.1
Lung ca. NCI-H522	17.6	Brain (Substantia nigra) Pool	9.1

Liver	5.3	Brain (Thalamus) Pool	13.1
Fetal Liver	21.6	Brain (whole)	18.4
Liver ca. HepG2	23.0	Spinal Cord Pool	6.6
Kidney Pool	22.1	Adrenal Gland	24.0
Fetal Kidney	24.1	Pituitary gland Pool	6.0
Renal ca. 786-0	20.9	Salivary Gland	13.3
Renal ca. A498	23.2	Thyroid (female)	9.5
Renal ca. ACHN	12.4	Pancreatic ca. CAPAN2	44.8
Renal ca. UO-31	27.7	Pancreas Pool	21.6

Table NE. Panel 1.2

Tissue Name	Rel. Exp.(%) Ag1179, Run 129140472	Tissue Name	Rel. Exp.(%) Ag1179, Run 129140472
Endothelial cells	6.0	Renal ca. 786-0	1.8
Heart (Fetal)	25.2	Renal ca. A498	16.6
Pancreas	3.5	Renal ca. RXF 393	0.6
Pancreatic ca. CAPAN 2	23.2	Renal ca. ACHN	8.0
Adrenal Gland	53.2	Renal ca. UO-31	5.0
Thyroid	6.2	Renal ca. TK-10	7.5
Salivary gland	26.4	Liver	15.6
Pituitary gland	14.4	Liver (fetal)	13.6
Brain (fetal)	17.9	Liver ca. (hepatoblast) HepG2	9.9
Brain (whole)	18.7	Lung	10.0
Brain (amygdala)	17.7	Lung (fetal)	13.6
Brain (cerebellum)	15.4	Lung ca. (small cell) LX-1	3.0
Brain (hippocampus)	31.0	Lung ca. (small cell) NCI-H69	3.5
Brain (thalamus)	9.3	Lung ca. (s.cell var.) SHP-77	4.6
Cerebral Cortex	47.0	Lung ca. (large cell) NCI-H460	100.0
Spinal cord	14.7	Lung ca. (non-sm. cell) A549	5.0
glio/astro U87-MG	8.7	Lung ca. (non-s.cell) NCI-H23	8.1
glio/astro U-118-MG	13.3	Lung ca. (non-s.cell) HOP-62	7.5
astrocytoma SW1783	4.7	Lung ca. (non-s.cl) NCI-H522	19.2
neuro*; met SK-N-AS	17.9	Lung ca. (squam.) SW 900	3.7
astrocytoma SF-539	1.7	Lung ca. (squam.) NCI-H596	8.0
astrocytoma SNB-75	2.2	Mammary gland	28.9
glioma SNB-19	9.0	Breast ca.* (pl.ef) MCF-7	8.2
glioma U251	3.1	Breast ca.* (pl.ef) MDA-MB-231	3.5
glioma SF-295	49.7	Breast ca.* (pl. ef) T47D	4.9
Heart	20.6	Breast ca. BT-549	11.7
Skeletal Muscle	6.2	Breast ca. MDA-N	4.8
Bone marrow	7.5	Ovary	34.9
Thymus	12.8	Ovarian ca. OVCAR-3	8.4
Spleen	9.3	Ovarian ca. OVCAR-4	12.0
Lymph node	42.0	Ovarian ca. OVCAR-5	9.7
Colorectal Tissue	10.8	Ovarian ca. OVCAR-8	1.6
Stomach	67.8	Ovarian ca. IGROV-1	8.6

Small intestine	20.3	Ovarian ca. (ascites) SK-OV-3	16.7
Colon ca. SW480	1.0	Uterus	9.2
Colon ca. * SW620 (SW480 met)	3.6	Placenta	31.2
Colon ca. HT29	1.3	Prostate	29.7
Colon ca. HCT-116	3.4	Prostate ca. * (bone met) PC-3	72.7
Colon ca. CaCo-2	7.2	Testis	45.4
Colon ca. Tissue (ODO3866)	6.6	Melanoma Hs688(A).T	4.9
Colon ca. HCC-2998	3.6	Melanoma* (met) Hs688(B).T	5.1
Gastric ca. * (liver met) NCI-N87	9.6	Melanoma UACC-62	34.9
Bladder	28.3	Melanoma M14	21.9
Trachea	16.8	Melanoma LOX IMVI	19.3
Kidney	4.6	Melanoma* (met) SK-MEL-5	25.5
Kidney (fetal)	25.3		

Table NF. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1179, Run 139820117	Rel. Exp.(%) Ag3287, Run 164633941	Tissue Name	Rel. Exp.(%) Ag1179, Run 139820117	Rel. Exp.(%) Ag3287, Run 164633941
Secondary Th1 act	46.0	55.5	HUVEC IL-1beta	5.9	9.9
Secondary Th2 act	76.3	71.7	HUVEC IFN gamma	21.3	65.1
Secondary Tr1 act	38.4	49.7	HUVEC TNF alpha + IFN gamma	10.7	25.9
Secondary Th1 rest	15.0	18.2	HUVEC TNF alpha + IL4	17.1	23.5
Secondary Th2 rest	18.8	18.8	HUVEC IL-11	9.3	14.4
Secondary Tr1 rest	10.7	23.5	Lung Microvascular EC none	17.6	26.8
Primary Th1 act	59.5	52.1	Lung Microvascular EC TNFalpha + IL-1beta	10.9	21.0
Primary Th2 act	47.0	40.1	Microvascular Dermal EC none	37.9	26.1
Primary Tr1 act	75.3	68.8	Microvascular Dermal EC TNFalpha + IL-1beta	21.3	17.7
Primary Th1 rest	52.1	60.3	Bronchial epithelium TNFalpha + IL1beta	32.5	33.4
Primary Th2 rest	30.1	33.9	Small airway epithelium none	11.9	19.8
Primary Tr1 rest	25.3	25.7	Small airway epithelium TNFalpha + IL-1beta	58.6	73.2
CD45RA CD4 lymphocyte act	25.0	40.1	Coronary artery SMC rest	15.6	22.5
CD45RO CD4 lymphocyte act	56.3	63.7	Coronary artery SMC TNFalpha + IL-1beta	14.9	13.6
CD8 lymphocyte act	35.6	53.6	Astrocytes rest	15.2	21.8
Secondary CD8 lymphocyte rest	44.4	48.3	Astrocytes TNFalpha + IL-1beta	17.3	19.6
Secondary CD8 lymphocyte act	29.1	21.3	KU-812 (Basophil) rest	39.0	59.9
CD4 lymphocyte none	16.5	22.5	KU-812 (Basophil) PMA/ionomycin	83.5	83.5
2ry Th1/Th2/Tr1_anti-	31.4	25.2	CCD1106	16.4	24.1

CD95 CH11			(Keratinocytes) none		
LAK cells rest	40.6	43.8	CCD1106 (Keratinocytes) TNFalpha + IL-1 beta	54.7	25.0
LAK cells IL-2	37.1	42.6	Liver cirrhosis	6.0	6.8
LAK cells IL-2+IL-12	35.8	34.2	Lupus kidney	17.1	10.4
LAK cells IL-2+IFN gamma	39.8	42.0	NCI-H292 none	29.5	35.4
LAK cells IL-2+ IL- 18	28.3	42.0	NCI-H292 IL-4	41.8	73.2
LAK cells PMA/ionomycin	18.4	19.8	NCI-H292 IL-9	35.4	48.6
NK Cells IL-2 rest	18.3	26.2	NCI-H292 IL-13	39.8	40.9
Two Way MLR 3 day	27.9	50.0	NCI-H292 IFN gamma	24.5	48.3
Two Way MLR 5 day	21.9	29.5	HPAEC none	20.0	29.5
Two Way MLR 7 day	19.3	19.6	HPAEC TNF alpha + IL-1 beta	18.9	23.7
PBMC rest	10.8	11.5	Lung fibroblast none	20.0	22.8
PBMC PWM	100.0	94.6	Lung fibroblast TNF alpha + IL-1 beta	9.9	15.5
PBMC PHA-L	62.0	49.0	Lung fibroblast IL-4	26.2	42.0
Ramos (B cell) none	69.7	39.8	Lung fibroblast IL-9	19.3	28.5
Ramos (B cell) ionomycin	93.3	100.0	Lung fibroblast IL-13	41.5	27.9
B lymphocytes PWM	79.6	91.4	Lung fibroblast IFN gamma	34.6	43.5
B lymphocytes CD40L and IL-4	40.6	59.0	Dermal fibroblast CCD1070 rest	47.3	48.3
EOL-1 dbcAMP	43.2	76.3	Dermal fibroblast CCD1070 TNF alpha	47.6	67.4
EOL-1 dbcAMP PMA/ionomycin	28.9	23.8	Dermal fibroblast CCD1070 IL-1 beta	31.4	34.6
Dendritic cells none	30.8	36.3	Dermal fibroblast IFN gamma	10.2	18.6
Dendritic cells LPS	32.8	44.4	Dermal fibroblast IL-4	23.7	24.8
Dendritic cells anti- CD40	35.6	38.4	IBD Colitis 2	2.6	2.8
Monocytes rest	28.1	37.9	IBD Crohn's	1.1	1.4
Monocytes LPS	37.9	24.3	Colon	17.0	23.7
Macrophages rest	58.2	67.4	Lung	13.9	21.6
Macrophages LPS	69.3	40.9	Thymus	39.0	31.6
HUVEC none	18.7	23.5	Kidney	40.6	63.3
HUVEC starved	24.8	34.9			

CNS_neurodegeneration_v1.0 Summary: [Ag3287](#) This panel confirms the expression of this gene at low levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: [Ag3287](#) The CG57562-01 gene shows moderate to high expression in all samples on this panel, with the highest expression in breast

cancer cell line BT 549 (CT=25.0). The widespread expression of this gene suggests that the gene product may be involved in cell differentiation and growth.

This gene is also widely expressed among tissues with metabolic and endocrine function, including adipose, skeletal muscle, heart, pancreas, liver, adrenal gland, thyroid, and pituitary gland. This expression profile suggests that this gene product may also be involved in metabolic function and that therapeutic modulation of the expression or function of this gene may be effective in the treatment of metabolic disorders, such as obesity and diabetes.

The expression profile of this gene also shows widespread expression of this gene in the brain. This suggests that the protein encoded by this gene may be important for normal neurological function. Therefore, modulation of the function or expression of this gene may be effective in the treatment of neurodegenerative disorders, such as Alzheimer's disease and Parkinson's disease.

Panel 1.2 Summary: Ag1179 Results using the Ag1179 primer pair in this panel are in good agreement with the results using Ag3287 on panel 1.4. There is moderate to high expression in all samples on this panel, with the highest level of expression in lung cancer cell line NCI-H460 (CT=23.6). Please see General_screening_panel_v1.4 summary.

Panel 4D Summary: Ag1179/Ag3287 Results from two experiments using identical probe/primer sets are in excellent agreement. This gene is expressed at high to moderate levels in a wide range of cell types of significance in the immune response in health and disease. These cells include members of the T-cell, B-cell, endothelial cell, macrophage/monocyte, and peripheral blood mononuclear cell family, as well as epithelial and fibroblast cell types from lung and skin, and normal tissues represented by colon, lung, thymus and kidney. This ubiquitous pattern of expression suggests that this gene product may be involved in homeostatic processes for these and other cell types and tissues. This pattern is in agreement with the expression profile in General_screening_panel_v1.4 and also suggests a role for the gene product in cell survival and proliferation.

Therefore, modulation of the gene product with a functional therapeutic may lead to the alteration of functions associated with these cell types and lead to improvement of the symptoms of patients suffering from autoimmune and inflammatory diseases such as asthma, allergies, inflammatory bowel disease, lupus erythematosus, psoriasis, rheumatoid arthritis, and osteoarthritis.

Expression of NOV17/CG55914-01 was assessed using the primer-probe sets Ag4424 and Ag2842, described in Tables OA and OB. Results of the RTQ-PCR runs are shown in Tables OC, OD, OE, OF, OG and OH.

Table OA. Probe Name Ag4424

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ctgaaaggggtccaaggtacagt-3'	22	341	307
Probe	TET-5'-cttcaaaggggtgcaagccccaagtct-3'-TAMRA	26	374	308
Reverse	5'-gtactgccaggccttaacacctt-3'	22	413	308

5

Table OB. Probe Name Ag2842

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gaaaggggtccaaggtacagttc-3'	22	343	310
Probe	TET-5'-cttcaaaggggtgcaagccccaagtct-3'-TAMRA	26	374	311
Reverse	5'-caggcttaacaccttgtgaaag-3'	22	406	312

Table OC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag4424, Run 219941948	Tissue Name	Rel. Exp.(%) Ag4424, Run 219941948
Adipose	0.0	Renal ca. TK-10	6.4
Melanoma* Hs688(A).T	0.0	Bladder	0.3
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	0.0	Gastric ca. KATO III	0.2
Melanoma* LOXIMVI	0.0	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	1.1	Colon ca. SW480	0.0
Squamous cell carcinoma SCC-4	0.7	Colon ca.* (SW480 met) SW620	0.0
Testis Pool	4.2	Colon ca. HT29	0.0
Prostate ca.* (bone met) PC-3	5.5	Colon ca. HCT-116	0.0
Prostate Pool	1.1	Colon ca. CaCo-2	2.7
Placenta	0.0	Colon cancer tissue	0.0
Uterus Pool	0.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	100.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	7.4	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	0.0	Colon Pool	0.0
Ovarian ca. OVCAR-5	1.9	Small Intestine Pool	0.0
Ovarian ca. IGROV-1	0.0	Stomach Pool	0.4
Ovarian ca. OVCAR-8	3.7	Bone Marrow Pool	0.0
Ovary	0.9	Fetal Heart	0.0
Breast ca. MCF-7	1.7	Heart Pool	0.0
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	0.6
Breast ca. BT 549	0.4	Fetal Skeletal Muscle	0.0
Breast ca. T47D	3.6	Skeletal Muscle Pool	2.6
Breast ca. MDA-N	0.0	Spleen Pool	0.0
Breast Pool	0.8	Thymus Pool	0.0
Trachea	1.7	CNS cancer (glio/astro) U87-MG	0.0
Lung	2.0	CNS cancer (glio/astro) U-118-MG	0.0
Fetal Lung	0.3	CNS cancer (neuro;met) SK-N-AS	0.2

Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	0.6	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	5.5	CNS cancer (glio) SNB-19	0.0
Lung ca. SHP-77	4.3	CNS cancer (glio) SF-295	14.3
Lung ca. A549	1.8	Brain (Amygdala) Pool	1.0
Lung ca. NCI-H526	0.0	Brain (cerebellum)	0.0
Lung ca. NCI-H23	1.6	Brain (fetal)	0.8
Lung ca. NCI-H460	0.3	Brain (Hippocampus) Pool	0.0
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	3.0
Lung ca. NCI-H522	1.1	Brain (Substantia nigra) Pool	1.4
Liver	0.0	Brain (Thalamus) Pool	0.3
Fetal Liver	2.0	Brain (whole)	0.1
Liver ca. HepG2	0.0	Spinal Cord Pool	1.8
Kidney Pool	1.2	Adrenal Gland	0.0
Fetal Kidney	0.2	Pituitary gland Pool	0.4
Renal ca. 786-0	0.0	Salivary Gland	0.0
Renal ca. A498	0.0	Thyroid (female)	0.0
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.2	Pancreas Pool	1.0

Table OD. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag2842, Run 161559587	Rel. Exp.(%) Ag2842, Run 165701935	Tissue Name	Rel. Exp.(%) Ag2842, Run 161559587	Rel. Exp.(%) Ag2842, Run 165701935
Liver adenocarcinoma	0.0	0.0	Kidney (fetal)	0.0	0.0
Pancreas	0.0	0.0	Renal ca. 786-0	0.0	0.0
Pancreatic ca. CAPAN 2	0.0	0.0	Renal ca. A498	0.0	0.0
Adrenal gland	0.0	0.0	Renal ca. RXF 393	0.0	0.0
Thyroid	0.0	0.0	Renal ca. ACHN	0.0	0.0
Salivary gland	0.0	0.0	Renal ca. UO-31	0.0	0.0
Pituitary gland	0.0	0.0	Renal ca. TK-10	0.0	24.0
Brain (fetal)	0.0	0.0	Liver	0.0	10.4
Brain (whole)	0.0	0.0	Liver (fetal)	0.0	0.0
Brain (amygdala)	7.8	0.0	Liver ca. (hepatoblast) HepG2	0.0	0.0
Brain (cerebellum)	0.0	0.0	Lung	0.0	0.0
Brain (hippocampus)	0.0	0.0	Lung (fetal)	0.0	0.0
Brain (substantia nigra)	0.0	0.0	Lung ca. (small cell) LX-1	0.0	0.0
Brain (thalamus)	0.0	9.3	Lung ca. (small cell) NCI-H69	30.8	0.0
Cerebral Cortex	6.3	7.4	Lung ca. (s.cell var.) SHP-77	19.1	9.6
Spinal cord	0.0	0.0	Lung ca. (large cell)NCI-H460	0.0	9.6
glio/astro U87-MG	0.0	0.0	Lung ca. (non-sm. cell) A549	0.0	6.9
glio/astro U-118-MG	0.0	0.0	Lung ca. (non- s.cell) NCI-H23	0.0	18.0
astrocytoma SW1783	0.0	0.0	Lung ca. (non- s.cell) HOP-62	0.0	0.0
neuro*; met SK-N-AS	0.0	6.0	Lung ca. (non-s.cl) NCI-H522	0.0	4.8
astrocytoma SF-539	0.0	0.0	Lung ca. (squam.)	5.4	17.6

			SW 900		
astrocytoma SNB-75	5.4	9.4	Lung ca. (squam.) NCI-H596	44.8	100.0
glioma SNB-19	0.0	0.0	Mammary gland	5.8	0.0
glioma U251	5.3	0.0	Breast ca.* (pl.ef) MCF-7	0.0	0.0
glioma SF-295	0.0	30.1	Breast ca.* (pl.ef) MDA-MB-231	0.0	0.0
Heart (fetal)	0.0	0.0	Breast ca.* (pl.ef) T47D	0.0	0.0
Heart	0.0	0.0	Breast ca. BT-549	0.0	0.0
Skeletal muscle (fetal)	8.8	0.0	Breast ca. MDA-N	0.0	0.0
Skeletal muscle	6.0	14.7	Ovary	0.0	0.0
Bone marrow	0.0	0.0	Ovarian ca. OVCAR-3	100.0	64.6
Thymus	0.0	0.0	Ovarian ca. OVCAR-4	0.0	7.7
Spleen	0.0	0.0	Ovarian ca. OVCAR-5	0.0	0.0
Lymph node	0.0	0.0	Ovarian ca. OVCAR-8	42.3	33.9
Colorectal	7.8	8.5	Ovarian ca. IGROV-1	0.0	0.0
Stomach	0.0	0.0	Ovarian ca.* (ascites) SK-OV-3	49.3	9.3
Small intestine	0.0	0.0	Uterus	0.0	0.0
Colon ca. SW480	0.0	0.0	Placenta	0.0	0.0
Colon ca.* SW620(SW480 met)	0.0	0.0	Prostate	4.7	0.0
Colon ca. HT29	0.0	0.0	Prostate ca.* (bone met)PC-3	3.9	6.2
Colon ca. HCT-116	0.0	0.0	Testis	39.8	7.5
Colon ca. CaCo-2	5.7	0.0	Melanoma Hs688(A).T	0.0	0.0
Colon ca. tissue(ODO3866)	0.0	0.0	Melanoma* (met) Hs688(B).T	0.0	0.0
Colon ca. HCC-2998	0.0	0.0	Melanoma UACC- 62	0.0	0.0
Gastric ca.* (liver met) NCI-N87	0.0	0.0	Melanoma M14	0.0	0.0
Bladder	2.4	0.0	Melanoma LOX IMVI	0.0	0.0
Trachea	0.0	0.0	Melanoma* (met) SK-MEL-5	2.7	0.0
Kidney	6.0	0.0	Adipose	0.0	0.0

Table OE. Panel 2D

Tissue Name	Rel. Exp.(%) Ag2842, Run 161559907	Tissue Name	Rel. Exp.(%) Ag2842, Run 161559907
Normal Colon	1.6	Kidney Margin 8120608	0.8
CC Well to Mod Diff (ODO3866)	0.9	Kidney Cancer 8120613	7.8
CC Margin (ODO3866)	0.0	Kidney Margin 8120614	3.3
CC Gr.2 rectosigmoid (ODO3868)	1.1	Kidney Cancer 9010320	4.1
CC Margin (ODO3868)	0.0	Kidney Margin 9010321	2.4
CC Mod Diff (ODO3920)	0.2	Normal Uterus	0.0
CC Margin (ODO3920)	0.5	Uterus Cancer 064011	1.6
CC Gr.2 ascend colon (ODO3921)	0.0	Normal Thyroid	1.5
CC Margin (ODO3921)	0.0	Thyroid Cancer 064010	0.9

CC from Partial Hepatectomy (ODO4309) Mets	2.8	Thyroid Cancer A302152	0.0
Liver Margin (ODO4309)	9.9	Thyroid Margin A302153	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Breast	2.1
Lung Margin (OD04451-02)	0.0	Breast Cancer (OD04566)	0.0
Normal Prostate 6546-1	0.8	Breast Cancer (OD04590-01)	24.0
Prostate Cancer (OD04410)	9.0	Breast Cancer Mets (OD04590-03)	16.5
Prostate Margin (OD04410)	0.0	Breast Cancer Metastasis (OD04655-05)	8.5
Prostate Cancer (OD04720-01)	3.8	Breast Cancer 064006	2.1
Prostate Margin (OD04720-02)	3.6	Breast Cancer 1024	2.2
Normal Lung 061010	1.9	Breast Cancer 9100266	1.8
Lung Met to Muscle (ODO4286)	2.4	Breast Margin 9100265	0.0
Muscle Margin (ODO4286)	0.9	Breast Cancer A209073	3.5
Lung Malignant Cancer (OD03126)	2.9	Breast Margin A209073	7.1
Lung Margin (OD03126)	0.7	Normal Liver	4.0
Lung Cancer (OD04404)	0.0	Liver Cancer 064003	2.6
Lung Margin (OD04404)	0.0	Liver Cancer 1025	1.8
Lung Cancer (OD04565)	2.5	Liver Cancer 1026	0.0
Lung Margin (OD04565)	0.0	Liver Cancer 6004-T	0.0
Lung Cancer (OD04237-01)	4.4	Liver Tissue 6004-N	3.0
Lung Margin (OD04237-02)	0.0	Liver Cancer 6005-T	0.0
Ocular Mel Met to Liver (ODO4310)	1.2	Liver Tissue 6005-N	0.0
Liver Margin (ODO4310)	6.8	Normal Bladder	1.9
Melanoma Mets to Lung (OD04321)	0.0	Bladder Cancer 1023	0.7
Lung Margin (OD04321)	0.0	Bladder Cancer A302173	6.0
Normal Kidney	14.6	Bladder Cancer (OD04718-01)	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	Bladder Normal Adjacent (OD04718-03)	0.0
Kidney Margin (OD04338)	4.7	Normal Ovary	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Ovarian Cancer 064008	12.6
Kidney Margin (OD04339)	4.0	Ovarian Cancer (OD04768-07)	100.0
Kidney Ca, Clear cell type (OD04340)	0.0	Ovary Margin (OD04768-08)	0.0
Kidney Margin (OD04340)	7.3	Normal Stomach	0.0
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 9060358	0.0
Kidney Margin (OD04348)	1.0	Stomach Margin 9060359	0.0
Kidney Cancer (OD04622-01)	0.0	Gastric Cancer 9060395	0.0
Kidney Margin (OD04622-03)	0.8	Stomach Margin 9060394	0.0
Kidney Cancer (OD04450-01)	0.7	Gastric Cancer 9060397	0.0
Kidney Margin (OD04450-03)	3.9	Stomach Margin 9060396	0.0
Kidney Cancer 8120607	0.0	Gastric Cancer 064005	0.0

Table OF. Panel 3D

Tissue Name	Rel. Exp.(%) Ag2842, Run 164843469	Tissue Name	Rel. Exp.(%) Ag2842, Run 164843469
Daoy- Medulloblastoma	0.0	Ca Ski- Cervical epidermoid carcinoma (metastasis)	0.0

TE671- Medulloblastoma	0.0	ES-2- Ovarian clear cell carcinoma	0.0
D283 Med- Medulloblastoma	0.0	Ramos- Stimulated with PMA/ionomycin 6h	0.0
PFSK-1- Primitive Neuroectodermal	0.0	Ramos- Stimulated with PMA/ionomycin 14h	0.0
XF-498- CNS	0.0	MEG-01- Chronic myelogenous leukemia (megakaryoblast)	0.0
SNB-78- Glioma	0.0	Raji- Burkitt's lymphoma	0.0
SF-268- Glioblastoma	0.0	Daudi- Burkitt's lymphoma	0.0
T98G- Glioblastoma	0.0	U266- B-cell plasmacytoma	33.4
SK-N-SH- Neuroblastoma (metastasis)	0.0	CA46- Burkitt's lymphoma	0.0
SF-295- Glioblastoma	0.0	RL- non-Hodgkin's B-cell lymphoma	0.0
Cerebellum	80.7	JM1- pre-B-cell lymphoma	0.0
Cerebellum	0.0	Jurkat- T cell leukemia	0.0
NCI-H292- Mucoepidermoid lung carcinoma	15.4	TF-1- Erythroleukemia	0.0
DMS-114- Small cell lung cancer	0.0	HUT 78- T-cell lymphoma	0.0
DMS-79- Small cell lung cancer	0.0	U937- Histiocytic lymphoma	0.0
NCI-H146- Small cell lung cancer	89.5	KU-812- Myelogenous leukemia	0.0
NCI-H526- Small cell lung cancer	0.0	769-P- Clear cell renal carcinoma	0.0
NCI-N417- Small cell lung cancer	0.0	Caki-2- Clear cell renal carcinoma	0.0
NCI-H82- Small cell lung cancer	0.0	SW 839- Clear cell renal carcinoma	1.8
NCI-H157- Squamous cell lung cancer (metastasis)	0.0	G401- Wilms' tumor	0.0
NCI-H1155- Large cell lung cancer	13.2	Hs766T- Pancreatic carcinoma (LN metastasis)	0.0
NCI-H1299- Large cell lung cancer	0.0	CAPAN-1- Pancreatic adenocarcinoma (liver metastasis)	0.0
NCI-H727- Lung carcinoid	0.0	SU86.86- Pancreatic carcinoma (liver metastasis)	0.0
NCI-UMC-11- Lung carcinoid	54.0	BxPC-3- Pancreatic adenocarcinoma	0.0
LX-1- Small cell lung cancer	0.0	HPAC- Pancreatic adenocarcinoma	0.0
Colo-205- Colon cancer	0.0	MIA PaCa-2- Pancreatic carcinoma	0.0
KM12- Colon cancer	0.0	CFPAC-1- Pancreatic ductal adenocarcinoma	59.9
KM20L2- Colon cancer	0.0	PANC-1- Pancreatic epithelioid ductal carcinoma	0.0
NCI-H716- Colon cancer	0.0	T24- Bladder carcinoma (transitional cell)	0.0
SW-48- Colon adenocarcinoma	0.0	5637- Bladder carcinoma	7.2
SW1116- Colon adenocarcinoma	0.0	HT-1197- Bladder carcinoma	36.6
LS 174T- Colon adenocarcinoma	0.0	UM-UC-3- Bladder carcinoma (transitional cell)	0.0
SW-948- Colon adenocarcinoma	0.0	A204- Rhabdomyosarcoma	0.0
SW-480- Colon adenocarcinoma	0.0	HT-1080- Fibrosarcoma	100.0
NCI-SNU-5- Gastric carcinoma	0.0	MG-63- Osteosarcoma	0.0
KATO III- Gastric carcinoma	0.0	SK-LMS-1- Leiomyosarcoma (vulva)	0.0
NCI-SNU-16- Gastric carcinoma	0.0	SJRH30- Rhabdomyosarcoma (met to bone marrow)	0.0
NCI-SNU-1- Gastric carcinoma	0.0	A431- Epidermoid carcinoma	0.0
RF-1- Gastric adenocarcinoma	0.0	WM266-4- Melanoma	0.0
RF-48- Gastric adenocarcinoma	0.0	DU 145- Prostate carcinoma (brain metastasis)	0.0

Tissue Name	Rel. Exp.(%) Ag2842, Run 159841917	Tissue Name	Rel. Exp.(%) Ag2842, Run 159841917
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microsvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronery artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronery artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	0.0
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	100.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.1
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0

PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	1.1	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	0.1
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Table OH. Panel 5D

Tissue Name	Rel. Exp.(%) Ag2842, Run 223784832	Tissue Name	Rel. Exp.(%) Ag2842, Run 223784832
97457_Patient-02go_adipose	0.0	94709_Donor 2 AM - A_adipose	0.0
97476_Patient-07sk_skeletal muscle	0.0	94710_Donor 2 AM - B_adipose	0.0
97477_Patient-07ut_uterus	0.0	94711_Donor 2 AM - C_adipose	0.0
97478_Patient-07pl_placenta	0.0	94712_Donor 2 AD - A_adipose	0.0
97481_Patient-08sk_skeletal muscle	0.0	94713_Donor 2 AD - B_adipose	0.0
97482_Patient-08ut_uterus	0.0	94714_Donor 2 AD - C_adipose	29.9
97483_Patient-08pl_placenta	0.0	94742_Donor 3 U - A_Mesenchymal Stem Cells	0.0
97486_Patient-09sk_skeletal muscle	0.0	94743_Donor 3 U - B_Mesenchymal Stem Cells	0.0
97487_Patient-09ut_uterus	0.0	94730_Donor 3 AM - A_adipose	0.0
97488_Patient-09pl_placenta	0.0	94731_Donor 3 AM - B_adipose	0.0
97492_Patient-10ut_uterus	25.9	94732_Donor 3 AM - C_adipose	0.0
97493_Patient-10pl_placenta	0.0	94733_Donor 3 AD - A_adipose	0.0
97495_Patient-11go_adipose	0.0	94734_Donor 3 AD - B_adipose	0.0
97496_Patient-11sk_skeletal muscle	0.0	94735_Donor 3 AD - C_adipose	0.0
97497_Patient-11ut_uterus	0.0	77138_Liver_HepG2untreated	0.0
97498_Patient-11pl_placenta	0.0	73556_Heart_Cardiac stromal cells (primary)	0.0
97500_Patient-12go_adipose	0.0	81735_Small Intestine	0.0
97501_Patient-12sk_skeletal muscle	100.0	72409_Kidney_Proximal Convoluted Tubule	0.0
97502_Patient-12ut_uterus	0.0	82685_Small intestine_Duodenum	33.4
97503_Patient-12pl_placenta	0.0	90650_Adrenal_Adrenocortical adenoma	0.0
94721_Donor 2 U - A_Mesenchymal Stem Cells	0.0	72410_Kidney_HRCE	0.0
94722_Donor 2 U - B_Mesenchymal Stem Cells	0.0	72411_Kidney_HRE	0.0
94723_Donor 2 U - C_Mesenchymal Stem Cells	0.0	73139_Uterus_Uterine smooth muscle cells	0.0

General_screening_panel_v1.4 Summary: Ag4424 Expression of the CG55914-01 gene is highest in ovarian cancer cell line OVCAR-3 (CT=29.5). Therefore, expression of this gene can be used to distinguish this cell line from the other samples on this panel. In addition, there is low but significant expression of this gene associated with an additional ovarian cancer and two lung cancer cell lines. Therefore, therapeutic modulation of the activity of this gene or its protein product, through the use of small molecule drugs, protein therapeutics or antibodies, might be beneficial in the treatment of lung cancer or ovarian cancer.

Panel 1.3D Summary: Ag2842 Results from two experiments using the same probe/primer pair gave similar results. Expression of the CG55914-01 gene is highest in ovarian and lung cancer cell lines, consistent with what is observed in General_screening_panel_v1.4.

Panel 2D Summary: Ag2842 Expression of this gene is highest in an ovarian cancer sample (CT = 30.5) and is significantly higher than in the matched normal ovarian tissue. In addition, this gene is expressed at significant levels in another ovarian tumor. Therefore, expression of this gene may be used to distinguish ovarian cancers from the other samples on this panel. Furthermore, therapeutic modulation of the activity of the protein encoded by this gene may be beneficial in the treatment of ovarian cancer.

Panel 3D Summary: Ag2842 This gene is expressed at low levels in a number of cancer cell lines including fibrosarcoma, lung cancer and pancreatic ductal adenocarcinoma. Therefore, expression of this gene may play a role in these types of cancers.

Panel 4D Summary: Ag2842 Expression of the CG55914-01 gene is highest in stimulated lymphokine-activated killer (LAK) cells (CT = 24.3). Therefore, expression of this gene can be used to distinguish this sample from the other samples on this panel. Since LAK cells are involved in tumor immunology and tumor cell clearance, as well as virally and bacterial infected cells, therapeutic modulation of this gene product may alter the functions of these cells and lead to improvement in cancer cell killing as well as host immunity to microbial and viral infections.

Panel 5D Summary: Ag2842 Results from one experiment with the CG55914-01 gene are not included. The amp plot indicates that there were experimental difficulties with this run.

NOV18

Expression of NOV18/CG57328-01 was assessed using the primer-probe set Ag3200, described in Table PA. Results of the RTQ-PCR runs are shown in Table PB.

Small intestine	2.0	Uterus	0.0
Colon ca. SW480	0.0	Placenta	0.0
Colon ca. * SW620(SW480 met)	3.1	Prostate	1.9
Colon ca. HT29	1.6	Prostate ca. * (bone met)PC-3	2.3
Colon ca. HCT-116	2.0	Testis	1.9
Colon ca. CaCo-2	5.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.7	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	7.8	Melanoma UACC-62	0.0
Gastric ca. * (liver met) NCI-N87	8.9	Melanoma M14	0.0
Bladder	3.1	Melanoma LOX IMVI	0.0
Trachea	2.2	Melanoma* (met) SK-MEL-5	0.4
Kidney	0.0	Adipose	2.3

Panel 1.3D Summary: Ag3200 Significant expression of the CG57328-01 gene is restricted to two lung cancer cell lines (CT = 32-33). Thus, expression of this gene could be used to distinguish these samples from the other samples in the panel. In addition, therapeutic modulation of the activity of this gene or its protein product, through the use of small molecule drugs, protein therapeutics or antibodies, might be beneficial in the treatment of lung cancer.

NOV19

Expression of NOV19 CG57358-01 was assessed using the primer-probe set Ag3214, described in Table QA. Results of the RTQ-PCR runs are shown in Tables QB, QC, QD and QE.

Table QA. Probe Name Ag3214

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ttcaacaggaagggtgatttca-3'	22	520	316
Probe	TET-5'-attttctctggtcggccgtcacctt-3'-TAMRA	26	550	317
Reverse	5'-aagtactgctggggaatgaag-3'	21	585	318

Table QB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3214, Run 209861781	Tissue Name	Rel. Exp.(%) Ag3214, Run 209861781
AD 1 Hippo	19.5	Control (Path) 3 Temporal Ctx	5.4
AD 2 Hippo	23.5	Control (Path) 4 Temporal Ctx	25.9
AD 3 Hippo	14.8	AD 1 Occipital Ctx	19.3
AD 4 Hippo	8.5	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	100.0	AD 3 Occipital Ctx	9.3
AD 6 Hippo	48.0	AD 4 Occipital Ctx	20.2
Control 2 Hippo	36.6	AD 5 Occipital Ctx	50.0
Control 4 Hippo	10.3	AD 6 Occipital Ctx	30.6
Control (Path) 3 Hippo	10.3	Control 1 Occipital Ctx	8.6

AD 1 Temporal Ctx	24.7	Control 2 Occipital Ctx	68.8
AD 2 Temporal Ctx	28.7	Control 3 Occipital Ctx	27.0
AD 3 Temporal Ctx	8.7	Control 4 Occipital Ctx	11.6
AD 4 Temporal Ctx	23.7	Control (Path) 1 Occipital Ctx	81.8
AD 5 Inf Temporal Ctx	95.3	Control (Path) 2 Occipital Ctx	14.8
AD 5 Sup Temporal Ctx	55.9	Control (Path) 3 Occipital Ctx	7.0
AD 6 Inf Temporal Ctx	52.9	Control (Path) 4 Occipital Ctx	17.0
AD 6 Sup Temporal Ctx	46.3	Control 1 Parietal Ctx	13.2
Control 1 Temporal Ctx	7.9	Control 2 Parietal Ctx	33.7
Control 2 Temporal Ctx	52.5	Control 3 Parietal Ctx	18.8
Control 3 Temporal Ctx	18.8	Control (Path) 1 Parietal Ctx	68.3
Control 3 Temporal Ctx	9.0	Control (Path) 2 Parietal Ctx	21.0
Control (Path) 1 Temporal Ctx	52.1	Control (Path) 3 Parietal Ctx	5.6
Control (Path) 2 Temporal Ctx	26.6	Control (Path) 4 Parietal Ctx	38.2

Table QC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag3214, Run 168012858	Tissue Name	Rel. Exp.(%) Ag3214, Run 168012858
Liver adenocarcinoma	0.4	Kidney (fetal)	18.8
Pancreas	3.1	Renal ca. 786-0	4.3
Pancreatic ca. CAPAN 2	5.8	Renal ca. A498	0.6
Adrenal gland	0.8	Renal ca. RXF 393	24.1
Thyroid	0.7	Renal ca. ACHN	75.3
Salivary gland	3.5	Renal ca. UO-31	3.0
Pituitary gland	0.7	Renal ca. TK-10	3.2
Brain (fetal)	7.3	Liver	1.5
Brain (whole)	21.9	Liver (fetal)	1.1
Brain (amygdala)	14.8	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	9.0	Lung	16.6
Brain (hippocampus)	10.8	Lung (fetal)	14.3
Brain (substantia nigra)	12.9	Lung ca. (small cell) LX-1	78.5
Brain (thalamus)	14.4	Lung ca. (small cell) NCI-H69	1.5
Cerebral Cortex	24.5	Lung ca. (s.cell var.) SHP-77	10.8
Spinal cord	6.7	Lung ca. (large cell) NCI-H460	0.2
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.4
glio/astro U-118-MG	0.9	Lung ca. (non-s.cell) NCI-H23	0.1
astrocytoma SW1783	0.1	Lung ca. (non-s.cell) HOP-62	0.1
neuro*; met SK-N-AS	0.1	Lung ca. (non-s.cl) NCI-H522	0.2
astrocytoma SF-539	0.9	Lung ca. (squam.) SW 900	8.4
astrocytoma SNB-75	4.7	Lung ca. (squam.) NCI-H596	0.9

glioma SNB-19	0.1	Mammary gland	4.7
glioma U251	0.1	Breast ca. * (pl.ef) MCF-7	1.3
glioma SF-295	0.1	Breast ca. * (pl.ef) MDA-MB-231	4.5
Heart (fetal)	13.3	Breast ca. * (pl.ef) T47D	6.6
Heart	3.6	Breast ca. BT-549	0.1
Skeletal muscle (fetal)	6.2	Breast ca. MDA-N	0.2
Skeletal muscle	1.5	Ovary	1.3
Bone marrow	1.7	Ovarian ca. OVCAR-3	0.0
Thymus	1.3	Ovarian ca. OVCAR-4	13.3
Spleen	3.0	Ovarian ca. OVCAR-5	98.6
Lymph node	5.0	Ovarian ca. OVCAR-8	0.2
Colorectal	1.0	Ovarian ca. IGROV-1	8.4
Stomach	3.3	Ovarian ca. * (ascites) SK-OV-3	0.1
Small intestine	3.8	Uterus	3.1
Colon ca. SW480	3.6	Placenta	1.0
Colon ca. * SW620(SW480 met)	100.0	Prostate	0.6
Colon ca. HT29	13.0	Prostate ca. * (bone met)PC-3	0.0
Colon ca. HCT-116	0.2	Testis	0.6
Colon ca. CaCo-2	0.1	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	16.2	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	28.9	Melanoma UACC-62	0.1
Gastric ca. * (liver met) NCI-N87	6.2	Melanoma M14	0.0
Bladder	11.0	Melanoma LOX IMVI	0.0
Trachea	2.1	Melanoma* (met) SK-MEL-5	0.2
Kidney	32.5	Adipose	3.9

Table QD. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag3214, Run 174416265	Tissue Name	Rel. Exp.(%) Ag3214, Run 174416265
Normal Colon	1.8	Kidney Margin (OD04348)	62.9
Colon cancer (OD06064)	37.6	Kidney malignant cancer (OD06204B)	0.8
Colon Margin (OD06064)	2.8	Kidney normal adjacent tissue (OD06204E)	26.4
Colon cancer (OD06159)	1.1	Kidney Cancer (OD04450-01)	33.9
Colon Margin (OD06159)	0.8	Kidney Margin (OD04450-03)	15.7
Colon cancer (OD06297-04)	1.9	Kidney Cancer 8120613	0.4
Colon Margin (OD06297-05)	2.1	Kidney Margin 8120614	58.6
CC Gr.2 ascend colon (ODO3921)	5.3	Kidney Cancer 9010320	3.5
CC Margin (ODO3921)	0.6	Kidney Margin 9010321	20.2
Colon cancer metastasis (OD06104)	3.4	Kidney Cancer 8120607	100.0
Lung Margin (OD06104)	3.2	Kidney Margin 8120608	47.6
Colon mets to lung (OD04451-01)	6.8	Normal Uterus	2.8
Lung Margin (OD04451-02)	5.0	Uterine Cancer 064011	1.1
Normal Prostate	0.4	Normal Thyroid	0.5
Prostate Cancer (OD04410)	1.1	Thyroid Cancer 064010	0.1

Prostate Margin (OD04410)	1.2	Thyroid Cancer A302152	2.0
Normal Ovary	1.4	Thyroid Margin A302153	0.7
Ovarian cancer (OD06283-03)	0.3	Normal Breast	1.7
Ovarian Margin (OD06283-07)	8.0	Breast Cancer (OD04566)	0.8
Ovarian Cancer 064008	1.7	Breast Cancer 1024	6.9
Ovarian cancer (OD06145)	1.1	Breast Cancer (OD04590-01)	3.0
Ovarian Margin (OD06145)	2.2	Breast Cancer Mets (OD04590-03)	1.6
Ovarian cancer (OD06455-03)	6.5	Breast Cancer Metastasis (OD04655-05)	2.9
Ovarian Margin (OD06455-07)	1.3	Breast Cancer 064006	2.3
Normal Lung	5.7	Breast Cancer 9100266	1.4
Invasive poor diff. lung adeno (ODO4945-01)	0.2	Breast Margin 9100265	1.1
Lung Margin (ODO4945-03)	6.2	Breast Cancer A209073	1.9
Lung Malignant Cancer (OD03126)	15.6	Breast Margin A2090734	2.1
Lung Margin (OD03126)	3.2	Breast cancer (OD06083)	11.9
Lung Cancer (OD05014A)	1.3	Breast cancer node metastasis (OD06083)	11.2
Lung Margin (OD05014B)	3.5	Normal Liver	1.9
Lung cancer (OD06081)	1.4	Liver Cancer 1026	2.5
Lung Margin (OD06081)	4.9	Liver Cancer 1025	3.1
Lung Cancer (OD04237-01)	1.0	Liver Cancer 6004-T	1.8
Lung Margin (OD04237-02)	12.3	Liver Tissue 6004-N	0.0
Ocular Melanoma Metastasis	0.0	Liver Cancer 6005-T	2.2
Ocular Melanoma Margin (Liver)	1.0	Liver Tissue 6005-N	11.2
Melanoma Metastasis	0.2	Liver Cancer 064003	1.0
Melanoma Margin (Lung)	4.2	Normal Bladder	8.1
Normal Kidney	9.1	Bladder Cancer 1023	4.1
Kidney Ca, Nuclear grade 2 (OD04338)	24.8	Bladder Cancer A302173	0.6
Kidney Margin (OD04338)	11.7	Normal Stomach	3.8
Kidney Ca Nuclear grade 1/2 (OD04339)	5.1	Gastric Cancer 9060397	15.2
Kidney Margin (OD04339)	23.0	Stomach Margin 9060396	11.7
Kidney Ca, Clear cell type (OD04340)	14.1	Gastric Cancer 9060395	7.1
Kidney Margin (OD04340)	16.6	Stomach Margin 9060394	17.2
Kidney Ca, Nuclear grade 3 (OD04348)	0.7	Gastric Cancer 064005	3.7

Table OE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3214, Run 164682510	Tissue Name	Rel. Exp.(%) Ag3214, Run 164682510
Secondary Th1 act	0.3	HUVEC IL-1beta	3.5
Secondary Th2 act	0.2	HUVEC IFN gamma	14.4
Secondary Tr1 act	0.6	HUVEC TNF alpha + IFN gamma	6.0
Secondary Th1 rest	0.5	HUVEC TNF alpha + IL4	5.8
Secondary Th2 rest	1.4	HUVEC IL-11	24.8
Secondary Tr1 rest	1.1	Lung Microvascular EC none	50.0
Primary Th1 act	0.2	Lung Microvascular EC TNFalpha + IL-1beta	40.6
Primary Th2 act	0.1	Microvascular Dermal EC none	32.1
Primary Tr1 act	0.0	Microvascular Dermal EC	24.8

		TNFalpha + IL-1beta	
Primary Th1 rest	0.8	Bronchial epithelium TNFalpha + IL1beta	3.0
Primary Th2 rest	0.7	Small airway epithelium none	9.0
Primary Tr1 rest	1.6	Small airway epithelium TNFalpha + IL-1beta	19.6
CD45RA CD4 lymphocyte act	0.1	Coronary artery SMC rest	0.2
CD45RO CD4 lymphocyte act	0.3	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.1	Astrocytes rest	3.5
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	5.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.6
CD4 lymphocyte none	0.4	KU-812 (Basophil) PMA/ionomycin	0.4
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.9	CCD1106 (Keratinocytes) none	0.8
LAK cells rest	0.1	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.1
LAK cells IL-2	0.4	Liver cirrhosis	6.3
LAK cells IL-2+IL-12	0.2	Lupus kidney	6.1
LAK cells IL-2+IFN gamma	0.2	NCI-H292 none	1.3
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	1.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	2.2
NK Cells IL-2 rest	0.2	NCI-H292 IL-13	0.7
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	2.3
Two Way MLR 5 day	0.3	HPAEC none	15.4
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	2.1
PBMC rest	0.1	Lung fibroblast none	0.0
PBMC PWM	0.3	Lung fibroblast TNF alpha + IL-1 beta	0.1
PBMC PHA-L	0.6	Lung fibroblast IL-4	0.3
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.2	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.1	Lung fibroblast IFN gamma	0.1
B lymphocytes CD40L and IL-4	0.2	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	3.5	Dermal fibroblast CCD1070 TNF alpha	2.9
EOL-1 dbcAMP PMA/ionomycin	6.6	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.1	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.2	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.2	IBD Colitis 2	0.3
Monocytes rest	0.5	IBD Crohn's	0.9
Monocytes LPS	0.1	Colon	9.1
Macrophages rest	0.1	Lung	20.0
Macrophages LPS	0.0	Thymus	100.0
HUVEC none	12.1	Kidney	5.8
HUVEC starved	23.5		

CNS_neurodegeneration_v1.0 Summary: Ag3214 This panel confirms the expression of this gene at low levels in the brain in an independent group of individuals.

However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.3D for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

5 **Panel 1.3D Summary:** Ag3214 Expression of the CG57358-01 gene is highest in colon cancer cell line SW620 and an ovarian cancer cell line (CTs = 26.1). It is expressed in a number of cancer cell lines including ovarian, breast, lung, renal, liver adenocarcinoma, and astrocytoma. Therefore, this gene may play a role in these types of cancer.

10 This gene is expressed at moderate levels throughout the CNS, including in amygdala, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression. The CG57358-01 gene encodes a protein with similarity to the Drosophila spinster gene. Expression of the CG57358-01 gene in brain is consistent with observations made on the Drosophila spinster gene.

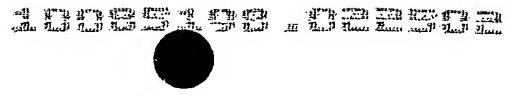
15 Mutations of the spinster gene in Drosophila cause degeneration of adults neurons and reductions in programmed neuronal cell death (ref. 1). Thus, modulation of expression of the CG57358-01 gene may be important in the treatment of neurodegenerative diseases and aging.

20 Among tissues with metabolic or endocrine function, this gene is expressed at moderate levels in adipose, pancreas, liver, skeletal muscle, and heart and at low levels in thyroid, adrenal gland and pituitary gland. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

References:

25 1. Nakano Y, Fujitani K, Kurihara J, Ragan J, Usui-Aoki K, Shimoda L, Lukacsovich T, Suzuki K, Sezaki M, Sano Y, Ueda R, Awano W, Kaneda M, Umeda M, Yamamoto D. Mutations in the novel membrane protein spinster interfere with programmed cell death and cause neural degeneration in Drosophila melanogaster. Mol Cell Biol 2001 Jun;21(11):3775-88.

30 Mutations in the spin gene are characterized by an extraordinarily strong rejection behavior of female flies in response to male courtship. They are also accompanied by decreases in the viability, adult life span, and oviposition rate of the flies. In spin mutants, some oocytes and adult neural cells undergo degeneration, which is preceded by reductions in programmed cell death of nurse cells in ovaries and of neurons in the pupal nervous system,



respectively. The central nervous system (CNS) of spin mutant flies accumulates autofluorescent lipopigments with characteristics similar to those of lipofuscin. The spin locus generates at least five different transcripts, with only two of these being able to rescue the spin behavioral phenotype; each encodes a protein with multiple membrane-spanning domains that are expressed in both the surface glial cells in the CNS and the follicle cells in the ovaries. Orthologs of the spin gene have also been identified in a number of species from nematodes to humans. Analysis of the spin mutant will give us new insights into neurodegenerative diseases and aging.

PMID: 11340170

Panel 2.2 Summary: Ag3214 Expression of the CG57358-01 gene is highest in a kidney cancer sample (CT = 28.4). However, in general expression of this gene appears to be higher in matched normal kidney and lung tissues when compared to the adjacent tumors. Therefore, therapeutic modulation of the activity of this gene or its protein product, using small molecule drugs, antibodies or protein therapeutics, may be of use in the treatment of kidney and lung cancer.

Panel 4D Summary: Ag3214 Expression of the CG57358-01 gene is highest in thymus (CT = 27). In addition, low levels of expression of this gene are detected in resting T cells. Therefore, small molecule therapeutics or antibody therapeutics designed against the protein encoded for by this gene could be utilized to modulate immune function (T cell development) and be important for organ transplant, AIDS treatment or post chemotherapy immune reconstitution.

Expression of this gene is also detected at moderate levels in a number of endothelial cell samples on this panel including lung microvascular endothelial cells, microvascular dermal endothelial cells, HPAEC and HUVECs, suggesting a role for this gene in endothelium integrity or homeostasis. Thus, this gene may play a role in inflammation. Therefore, therapeutic modulation of the activity of this gene, using small molecule drugs, antibodies or protein therapeutics, may be of use in the treatment or prevention of inflammatory reactions.

NOV20

Expression of NOV20/CG57695-01 was assessed using the primer-probe set Ag3310, described in Table RA. Results of the RTQ-PCR run are shown in Tables RB.

Table RA. Probe Name Ag3310

Primers	Sequences	Length	Start Position	SEQ ID NO
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Fetal Kidney	7.5	Pituitary gland Pool	0.0
Renal ca. 786-0	0.0	Salivary Gland	0.0
Renal ca. A498	0.0	Thyroid (female)	0.0
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.0	Pancreas Pool	0.0

CNS_neurodegeneration_v1.0 Summary: Ag3310 Expression of the CG57695-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3310 Expression of the CG57695-01 gene is seen only in the testis (CT = 33.8) Therefore, expression of this gene can be used to distinguish testis from the other samples on this panel. In addition, therapeutic modulation of the activity of this gene may be of use in the treatment of reproductive disorders such as infertility.

Panel 4D Summary: Ag3310 Expression of the CG57695-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV21

Expression of NOV21/CG57654-01 was assessed using the primer-probe set Ag1680, described in Table SA. Results of the RTQ-PCR runs are shown in Tables SB, SC, SD and SE.

Table SA. Probe Name Ag1680

Primers	Sequences	Length	Start Position
Forward	5'-gccaaattacaattgcacaattt-3'	22	795
Probe	TET-5'-atgaacactcctgccccttgagggtt-3'-TAMRA	25	825
Reverse	5'-tcttcacgtggatagccataac-3'	22	855

Table SB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag1680, Run 207624859	Tissue Name	Rel. Exp.(%) Ag1680, Run 207624859
AD 1 Hippo	5.0	Control (Path) 3 Temporal Ctx	0.8
AD 2 Hippo	9.0	Control (Path) 4 Temporal Ctx	20.4
AD 3 Hippo	2.9	AD 1 Occipital Ctx	12.9
AD 4 Hippo	3.7	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	85.3	AD 3 Occipital Ctx	1.3
AD 6 Hippo	38.2	AD 4 Occipital Ctx	19.3
Control 2 Hippo	27.0	AD 5 Occipital Ctx	65.5
Control 4 Hippo	2.4	AD 6 Occipital Ctx	43.2
Control (Path) 3 Hippo	0.6	Control 1 Occipital Ctx	0.3
AD 1 Temporal Ctx	4.8	Control 2 Occipital Ctx	100.0
AD 2 Temporal Ctx	12.6	Control 3 Occipital Ctx	16.6
AD 3 Temporal Ctx	2.5	Control 4 Occipital Ctx	2.1
AD 4 Temporal Ctx	14.0	Control (Path) 1 Occipital Ctx	69.7

AD 5 Inf Temporal Ctx	68.3	Control (Path) 2 Occipital Ctx	12.8
AD 5 Sup Temporal Ctx	17.3	Control (Path) 3 Occipital Ctx	0.2
AD 6 Inf Temporal Ctx	47.6	Control (Path) 4 Occipital Ctx	10.2
AD 6 Sup Temporal Ctx	61.1	Control 1 Parietal Ctx	1.3
Control 1 Temporal Ctx	0.9	Control 2 Parietal Ctx	18.2
Control 2 Temporal Ctx	52.5	Control 3 Parietal Ctx	21.0
Control 3 Temporal Ctx	15.9	Control (Path) 1 Parietal Ctx	59.5
Control 3 Temporal Ctx	4.8	Control (Path) 2 Parietal Ctx	23.2
Control (Path) 1 Temporal Ctx	42.0	Control (Path) 3 Parietal Ctx	0.6
Control (Path) 2 Temporal Ctx	40.6	Control (Path) 4 Parietal Ctx	30.6

Table SC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1680, Run 158317296	Tissue Name	Rel. Exp.(%) Ag1680, Run 158317296
Liver adenocarcinoma	0.3	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.5	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	8.1	Renal ca. TK-10	0.0
Brain (fetal)	3.7	Liver	0.0
Brain (whole)	27.0	Liver (fetal)	0.0
Brain (amygdala)	25.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	17.4	Lung	0.0
Brain (hippocampus)	100.0	Lung (fetal)	0.0
Brain (substantia nigra)	2.4	Lung ca. (small cell) LX-1	0.6
Brain (thalamus)	14.6	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	83.5	Lung ca. (s.cell var.) SHP-77	4.2
Spinal cord	0.5	Lung ca. (large cell) NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	4.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.5

Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	1.3
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.3
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	0.0
Small intestine	0.2	Uterus	0.0
Colon ca. SW480	0.0	Placenta	0.1
Colon ca.* SW620(SW480 met)	0.9	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.7	Testis	0.1
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.2
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table SD. Panel 2D

Tissue Name	Rel. Exp.(%) Ag1680, Run 158318977	Tissue Name	Rel. Exp.(%) Ag1680, Run 158318977
Normal Colon	100.0	Kidney Margin 8120608	0.0
CC Well to Mod Diff (ODO3866)	0.0	Kidney Cancer 8120613	0.0
CC Margin (ODO3866)	8.7	Kidney Margin 8120614	0.0
CC Gr.2 rectosigmoid (ODO3868)	0.0	Kidney Cancer 9010320	85.3
CC Margin (ODO3868)	12.3	Kidney Margin 9010321	0.0
CC Mod Diff (ODO3920)	7.5	Normal Uterus	0.0
CC Margin (ODO3920)	35.4	Uterus Cancer 064011	0.0
CC Gr.2 ascend colon (ODO3921)	7.6	Normal Thyroid	0.0
CC Margin (ODO3921)	9.5	Thyroid Cancer 064010	0.0
CC from Partial Hepatectomy (ODO4309) Mets	0.0	Thyroid Cancer A302152	0.0
Liver Margin (ODO4309)	0.0	Thyroid Margin A302153	0.0
Colon mets to lung (OD04451-01)	0.0	Normal Breast	0.0
Lung Margin (OD04451-02)	0.0	Breast Cancer (OD04566)	0.0
Normal Prostate 6546-1	0.0	Breast Cancer (OD04590-01)	0.0
Prostate Cancer (OD04410)	0.0	Breast Cancer Mets (OD04590-03)	0.0
Prostate Margin (OD04410)	0.0	Breast Cancer Metastasis (OD04655-05)	7.7
Prostate Cancer (OD04720-01)	7.4	Breast Cancer 064006	0.0
Prostate Margin (OD04720-02)	12.6	Breast Cancer 1024	0.0
Normal Lung 061010	7.9	Breast Cancer 9100266	0.0
Lung Met to Muscle (ODO4286)	0.0	Breast Margin 9100265	0.0
Muscle Margin (ODO4286)	0.0	Breast Cancer A209073	0.0

Lung Malignant Cancer (OD03126)	0.0	Breast Margin A209073	0.0
Lung Margin (OD03126)	0.0	Normal Liver	0.0
Lung Cancer (OD04404)	0.0	Liver Cancer 064003	0.0
Lung Margin (OD04404)	0.0	Liver Cancer 1025	0.0
Lung Cancer (OD04565)	26.8	Liver Cancer 1026	0.0
Lung Margin (OD04565)	0.0	Liver Cancer 6004-T	0.0
Lung Cancer (OD04237-01)	0.0	Liver Tissue 6004-N	0.0
Lung Margin (OD04237-02)	0.0	Liver Cancer 6005-T	0.0
Ocular Mel Met to Liver (ODO4310)	0.0	Liver Tissue 6005-N	0.0
Liver Margin (ODO4310)	0.0	Normal Bladder	16.0
Melanoma Mets to Lung (OD04321)	0.0	Bladder Cancer 1023	0.0
Lung Margin (OD04321)	0.0	Bladder Cancer A302173	57.4
Normal Kidney	0.0	Bladder Cancer (OD04718-01)	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	Bladder Normal Adjacent (OD04718-03)	0.0
Kidney Margin (OD04338)	0.0	Normal Ovary	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	Ovarian Cancer 064008	43.2
Kidney Margin (OD04339)	0.0	Ovarian Cancer (OD04768-07)	0.0
Kidney Ca, Clear cell type (OD04340)	0.0	Ovary Margin (OD04768-08)	0.0
Kidney Margin (OD04340)	0.0	Normal Stomach	7.4
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 9060358	0.0
Kidney Margin (OD04348)	0.0	Stomach Margin 9060359	3.3
Kidney Cancer (OD04622-01)	0.0	Gastric Cancer 9060395	8.1
Kidney Margin (OD04622-03)	0.0	Stomach Margin 9060394	7.4
Kidney Cancer (OD04450-01)	0.0	Gastric Cancer 9060397	1.3
Kidney Margin (OD04450-03)	0.0	Stomach Margin 9060396	6.5
Kidney Cancer 8120607	0.0	Gastric Cancer 064005	0.0

Table SE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1680, Run 158320708	Tissue Name	Rel. Exp.(%) Ag1680, Run 158320708
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	0.0

CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	19.9
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	48.3
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	0.0
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	94.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	31.2
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	100.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	16.4
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	20.2
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	7.5
Monocytes rest	0.0	IBD Crohn's	36.1
Monocytes LPS	0.0	Colon	49.3
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag1680 This panel confirms the expression of this gene at moderate to high levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.3D for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

Panel 1.3D Summary: Ag1680 The CG57654-01 gene is expressed at high to moderate levels in all regions of the CNS examined, including in amygdala, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord with the highest levels in the hippocampus (CT = 26.3). Therefore, expression of this gene may be used to distinguish brain samples from the other samples on this panel. This gene encodes a novel splice variant of the gamma-aminobutyric-acid receptor gamma-2 subunit precursor (GABA-A Receptor) gene. Several drugs, including benzodiazepines, anticonvulsants, anaesthetics and neurosteroids interact with binding sites on GABA-A receptors (ref 1). Therefore, modulation of expression of this gene may be used for treatment of central nervous system disorders such as epilepsy, anxiety and alcoholism.

Among tissues with metabolic or endocrine function, this gene is expressed at low levels in adrenal gland and pituitary gland. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

References:

1. Smith TA. Type A gamma-aminobutyric acid (GABAA) receptor subunits and benzodiazepine binding: significance to clinical syndromes and their treatment. Br J Biomed Sci 2001;58(2):111-21.

Gamma (gamma)-aminobutyric acid (GABA) acting via GABAA receptors is the brain's major inhibitory neurotransmitter system and exerts a crucial role in regulating brain excitability. A number of drugs interact with binding sites on GABAA receptors, and these include benzodiazepines, anticonvulsants, anaesthetics and neurosteroids (e.g. the progesterone metabolite pregnalone). GABAA receptors comprise five subunits (19 are known currently), and are classified into three major groups (alpha, beta and gamma) and several minor ones. The subunit make-up of a receptor, particularly its alpha-subunit content, determines its pharmacological characteristics. Thus, receptors that include an alpha1 subunit have a benzodiazepine (BZ) type I (BZ[I]) pharmacology and bind zolpidem and CL218,872 with high affinity, whilst receptors with alpha2, alpha3 or alpha5 subunits have a BZ type II (BZ[II]) pharmacology and bind these drugs with low affinity. In contrast to receptors that contain alpha4 and alpha6 subunits, which are diazepam-insensitive, both BZ(I) and -(II) bind diazepam and other benzodiazepines. The ligand selectivity of receptor subunits assists in their characterisation. Using immunochemical and ligand-binding techniques, the subunit composition of GABAA receptors has been shown to exhibit a degree of brain regional

specificity. GABAA receptors are of great clinical significance in several disorders, including epilepsy, anxiety and alcoholism. In addition to treating epilepsy with drugs that target GABAA and BZ binding sites, epileptic lesions can be localised presurgically using radiolabelled BZ ligands. BZs are used commonly to treat anxiety, and studies suggest that BZ antagonists and inverse agonists (which induce the opposite effect to agonists at receptors) may be useful in alcohol rehabilitation.

Panel 2D Summary: Ag1680 Expression of the CG57654-01 gene is highest in a sample of normal colon tissues (CT = 33.6). There appears to be a general pattern of overexpression of this gene in the normal matched colon samples when compared to the adjacent colon tumors. Therefore, therapeutic modulation of the activity of this gene or its protein product, using small molecule drugs, antibodies or protein therapeutics, may be of use in the treatment of colon cancer.

Panel 4D Summary: Ag1680 Expression of the CG57654-01 gene is highest in the lung-derived mucoepidermoid cell line (CT = 34.7). Therefore, therapeutic modulation of the activity of this gene, using small molecule drugs or antibodies, may be of use in the treatment of asthma and emphysema.

NOV22

Expression of gene NOV22/CG57724-01 was assessed using the primer-probe set Ag3316, described in Table TA. Results of the RTQ-PCR runs are shown in Tables TB, TC and TD.

Table TA. Probe Name Ag3316

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-tagtcaagatgccacttctgt-3'	22	1175	322
Probe	TET-5'-actgcagactgctcactaccaccgag-3'-TAMRA	26	1206	323
Reverse	5'-cgtgtgctctcaattcataca-3'	21	1253	324

Table TB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3316, Run 210144080	Tissue Name	Rel. Exp.(%) Ag3316, Run 210144080
AD 1 Hippo	2.1	Control (Path) 3 Temporal Ctx	4.6
AD 2 Hippo	35.8	Control (Path) 4 Temporal Ctx	71.7
AD 3 Hippo	5.1	AD 1 Occipital Ctx	13.9
AD 4 Hippo	19.5	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	26.1	AD 3 Occipital Ctx	1.4
AD 6 Hippo	81.8	AD 4 Occipital Ctx	37.9
Control 2 Hippo	52.9	AD 5 Occipital Ctx	55.5

Control 4 Hippo	5.2	AD 6 Occipital Ctx	35.1
Control (Path) 3 Hippo	4.2	Control 1 Occipital Ctx	2.8
AD 1 Temporal Ctx	18.4	Control 2 Occipital Ctx	40.9
AD 2 Temporal Ctx	47.6	Control 3 Occipital Ctx	31.9
AD 3 Temporal Ctx	2.5	Control 4 Occipital Ctx	2.1
AD 4 Temporal Ctx	40.9	Control (Path) 1 Occipital Ctx	87.1
AD 5 Inf Temporal Ctx	74.2	Control (Path) 2 Occipital Ctx	17.2
AD 5 Sup Temporal Ctx	25.9	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	100.0	Control (Path) 4 Occipital Ctx	29.7
AD 6 Sup Temporal Ctx	88.3	Control 1 Parietal Ctx	6.2
Control 1 Temporal Ctx	5.8	Control 2 Parietal Ctx	25.9
Control 2 Temporal Ctx	46.7	Control 3 Parietal Ctx	23.0
Control 3 Temporal Ctx	54.3	Control (Path) 1 Parietal Ctx	57.0
Control 3 Temporal Ctx	5.7	Control (Path) 2 Parietal Ctx	34.4
Control (Path) 1 Temporal Ctx	85.3	Control (Path) 3 Parietal Ctx	2.8
Control (Path) 2 Temporal Ctx	59.9	Control (Path) 4 Parietal Ctx	53.2

Table TC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3316, Run 215678598	Tissue Name	Rel. Exp.(%) Ag3316, Run 215678598
Adipose	12.4	Renal ca. TK-10	0.4
Melanoma* Hs688(A).T	2.5	Bladder	8.1
Melanoma* Hs688(B).T	4.0	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	0.0	Gastric ca. KATO III	0.6
Melanoma* LOXIMVI	0.0	Colon ca. SW-948	2.7
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	0.0
Squamous cell carcinoma SCC-4	0.6	Colon ca. * (SW480 met) SW620	0.0
Testis Pool	28.5	Colon ca. HT29	3.0
Prostate ca.* (bone met) PC-3	8.8	Colon ca. HCT-116	0.0
Prostate Pool	11.3	Colon ca. CaCo-2	0.0
Placenta	7.2	Colon cancer tissue	4.3
Uterus Pool	1.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	8.5	Colon ca. Colo-205	0.6
Ovarian ca. SK-OV-3	4.6	Colon ca. SW-48	3.5
Ovarian ca. OVCAR-4	0.0	Colon Pool	3.7
Ovarian ca. OVCAR-5	2.2	Small Intestine Pool	10.2
Ovarian ca. IGROV-1	0.0	Stomach Pool	2.7
Ovarian ca. OVCAR-8	1.0	Bone Marrow Pool	3.6
Ovary	2.9	Fetal Heart	1.5
Breast ca. MCF-7	10.2	Heart Pool	2.6
Breast ca. MDA-MB-231	6.5	Lymph Node Pool	3.8
Breast ca. BT 549	12.1	Fetal Skeletal Muscle	1.7
Breast ca. T47D	2.7	Skeletal Muscle Pool	2.5
Breast ca. MDA-N	0.0	Spleen Pool	3.7
Breast Pool	4.5	Thymus Pool	8.4

Trachea	80.7	CNS cancer (glio/astro) U87-MG	0.2
Lung	2.1	CNS cancer (glio/astro) U-118-MG	0.4
Fetal Lung	29.3	CNS cancer (neuro;met) SK-N-AS	1.1
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	2.0	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	2.6	CNS cancer (glio) SNB-19	0.4
Lung ca. SHP-77	5.8	CNS cancer (glio) SF-295	0.2
Lung ca. A549	3.4	Brain (Amygdala) Pool	14.4
Lung ca. NCI-H526	2.7	Brain (cerebellum)	35.6
Lung ca. NCI-H23	100.0	Brain (fetal)	9.4
Lung ca. NCI-H460	0.0	Brain (Hippocampus) Pool	11.8
Lung ca. HOP-62	3.5	Cerebral Cortex Pool	18.0
Lung ca. NCI-H522	14.2	Brain (Substantia nigra) Pool	12.0
Liver	13.4	Brain (Thalamus) Pool	17.4
Fetal Liver	12.3	Brain (whole)	17.6
Liver ca. HepG2	0.0	Spinal Cord Pool	5.9
Kidney Pool	6.0	Adrenal Gland	22.5
Fetal Kidney	16.2	Pituitary gland Pool	31.0
Renal ca. 786-0	0.8	Salivary Gland	32.3
Renal ca. A498	4.9	Thyroid (female)	7.3
Renal ca. ACHN	4.2	Pancreatic ca. CAPAN2	10.2
Renal ca. UO-31	2.3	Pancreas Pool	8.0

Table TD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3316, Run 164683048	Tissue Name	Rel. Exp.(%) Ag3316, Run 164683048
Secondary Th1 act	46.0	HUVEC IL-1beta	7.8
Secondary Th2 act	60.7	HUVEC IFN gamma	5.0
Secondary Tr1 act	88.3	HUVEC TNF alpha + IFN gamma	2.2
Secondary Th1 rest	31.2	HUVEC TNF alpha + IL4	2.5
Secondary Th2 rest	57.4	HUVEC IL-11	2.4
Secondary Tr1 rest	72.7	Lung Microvascular EC none	7.5
Primary Th1 act	23.3	Lung Microvascular EC TNFalpha + IL-1beta	3.8
Primary Th2 act	59.5	Microvascular Dermal EC none	7.8
Primary Tr1 act	76.8	Microvascular Dermal EC TNFalpha + IL-1beta	2.7
Primary Th1 rest	90.1	Bronchial epithelium TNFalpha + IL1beta	8.8
Primary Th2 rest	87.7	Small airway epithelium none	2.7
Primary Tr1 rest	99.3	Small airway epithelium TNFalpha + IL-1beta	37.9
CD45RA CD4 lymphocyte act	5.3	Coronary artery SMC rest	2.2
CD45RO CD4 lymphocyte act	35.8	Coronary artery SMC TNFalpha + IL-1beta	4.5
CD8 lymphocyte act	16.5	Astrocytes rest	9.8
Secondary CD8 lymphocyte rest	38.2	Astrocytes TNFalpha + IL-1beta	2.2
Secondary CD8 lymphocyte act	14.7	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	18.9	KU-812 (Basophil) PMA/ionomycin	1.7

2ry Th1/Th2/Tr1_anti-CD95 CH11	100.0	CCD1106 (Keratinocytes) none	34.6
LAK cells rest	64.6	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	32.3
LAK cells IL-2	2.3	Liver cirrhosis	11.4
LAK cells IL-2+IL-12	19.3	Lupus kidney	10.7
LAK cells IL-2+IFN gamma	60.7	NCI-H292 none	25.0
LAK cells IL-2+ IL-18	34.4	NCI-H292 IL-4	20.7
LAK cells PMA/ionomycin	37.6	NCI-H292 IL-9	25.5
NK Cells IL-2 rest	6.1	NCI-H292 IL-13	7.6
Two Way MLR 3 day	8.9	NCI-H292 IFN gamma	7.0
Two Way MLR 5 day	2.0	HPAEC none	0.0
Two Way MLR 7 day	1.4	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	4.7	Lung fibroblast none	3.4
PBMC PWM	48.6	Lung fibroblast TNF alpha + IL-1 beta	5.1
PBMC PHA-L	33.4	Lung fibroblast IL-4	12.6
Ramos (B cell) none	0.0	Lung fibroblast IL-9	5.8
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	4.8
B lymphocytes PWM	68.8	Lung fibroblast IFN gamma	2.3
B lymphocytes CD40L and IL-4	33.2	Dermal fibroblast CCD1070 rest	20.7
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	64.6
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	2.2
Dendritic cells none	9.8	Dermal fibroblast IFN gamma	6.1
Dendritic cells LPS	6.3	Dermal fibroblast IL-4	8.2
Dendritic cells anti-CD40	14.5	IBD Colitis 2	0.0
Monocytes rest	41.2	IBD Crohn's	4.5
Monocytes LPS	0.0	Colon	16.7
Macrophages rest	4.6	Lung	8.5
Macrophages LPS	4.8	Thymus	93.3
HUVEC none	0.0	Kidney	17.1
HUVEC starved	12.4		

CNS_neurodegeneration_v1.0 Summary: Ag3316 This panel confirms the expression of this gene at low levels in the brain in an independent group of individuals.

However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3316 Expression of the CG57724-01 gene is highest in lung cancer cell line NCI-H23 (CT = 29.4). This gene is also expressed at moderate levels in all regions of the central nervous system examined, including in amygdala, cerebellum, hippocampus, cerebral cortex, substantia nigra, thalamus, and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

Among tissues with metabolic or endocrine function, this gene is expressed at moderate levels in adrenal gland and pituitary gland and at low levels in pancreas, thyroid, liver, and adipose. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

The CG57724-01 gene encodes a protein with homology to carboxylesterases. Carboxylesterases (CESs) catalyze the hydrolysis of a variety of compounds containing ester and amide bonds. They may also play an important role in lipid and drug metabolism by hydrolyzing endogenous long-chain fatty acid esters.

Panel 4D Summary: Ag3316 Moderate to low expression of this gene is found in a wide range of cells included in this panel, with a highest expression in activated T cells and in particular T regulatory cells (Tr1). This gene encodes for a carboxylesterase like protein, a protein that plays an important role in the metabolism of endogenous lipids. Therefore regulation of carboxylesterase gene expression may have physiological significance essential in T cell mediated diseases such as autoimmune diseases and allergies as well as in B cell disorders.

NOV25

Expression of gene NOV25/CG57503-01 was assessed using the primer-probe set Ag3258, described in Table UA. Results of the RTQ-PCR runs are shown in Tables UB, UC and UD.

Table UA. Probe Name Ag3258

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gagtcaccgtaaggctgtca-3'	20	1728	325
Probe	TET-5'-catcccttcgccatcacagtgttg-3'-TAMRA	25	1765	326
Reverse	5'-tctgtccagtacaggctgtctt-3'	22	1790	327

Table UB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3258, Run 209990877	Tissue Name	Rel. Exp.(%) Ag3258, Run 209990877
AD 1 Hippo	56.6	Control (Path) 3 Temporal Ctx	42.3
AD 2 Hippo	44.8	Control (Path) 4 Temporal Ctx	49.3
AD 3 Hippo	42.6	AD 1 Occipital Ctx	56.6
AD 4 Hippo	23.3	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	96.6	AD 3 Occipital Ctx	68.8
AD 6 Hippo	77.4	AD 4 Occipital Ctx	50.3
Control 2 Hippo	39.0	AD 5 Occipital Ctx	43.8

Control 4 Hippo	39.5	AD 6 Occipital Ctx	38.4
Control (Path) 3 Hippo	30.1	Control 1 Occipital Ctx	27.4
AD 1 Temporal Ctx	90.8	Control 2 Occipital Ctx	34.2
AD 2 Temporal Ctx	55.5	Control 3 Occipital Ctx	39.0
AD 3 Temporal Ctx	46.0	Control 4 Occipital Ctx	27.7
AD 4 Temporal Ctx	47.3	Control (Path) 1 Occipital Ctx	53.6
AD 5 Inf Temporal Ctx	100.0	Control (Path) 2 Occipital Ctx	23.0
AD 5 Sup Temporal Ctx	88.9	Control (Path) 3 Occipital Ctx	24.3
AD 6 Inf Temporal Ctx	79.6	Control (Path) 4 Occipital Ctx	19.1
AD 6 Sup Temporal Ctx	57.0	Control 1 Parietal Ctx	33.2
Control 1 Temporal Ctx	36.1	Control 2 Parietal Ctx	85.9
Control 2 Temporal Ctx	35.8	Control 3 Parietal Ctx	25.9
Control 3 Temporal Ctx	42.6	Control (Path) 1 Parietal Ctx	68.8
Control 3 Temporal Ctx	26.8	Control (Path) 2 Parietal Ctx	47.6
Control (Path) 1 Temporal Ctx	53.2	Control (Path) 3 Parietal Ctx	26.2
Control (Path) 2 Temporal Ctx	39.8	Control (Path) 4 Parietal Ctx	39.8

Table UC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3258, Run 214694854	Tissue Name	Rel. Exp.(%) Ag3258, Run 214694854
Adipose	4.6	Renal ca. TK-10	13.1
Melanoma* Hs688(A).T	13.3	Bladder	3.1
Melanoma* Hs688(B).T	7.3	Gastric ca. (liver met.) NCI-N87	1.5
Melanoma* M14	22.4	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	26.1	Colon ca. SW-948	6.7
Melanoma* SK-MEL-5	50.7	Colon ca. SW480	7.7
Squamous cell carcinoma SCC-4	11.8	Colon ca. * (SW480 met) SW620	17.8
Testis Pool	3.8	Colon ca. HT29	0.0
Prostate ca. * (bone met) PC-3	3.6	Colon ca. HCT-116	12.9
Prostate Pool	7.3	Colon ca. CaCo-2	19.8
Placenta	7.7	Colon cancer tissue	4.4
Uterus Pool	3.1	Colon ca. SW1116	0.9
Ovarian ca. OVCAR-3	4.5	Colon ca. Colo-205	56.3
Ovarian ca. SK-OV-3	10.7	Colon ca. SW-48	100.0
Ovarian ca. OVCAR-4	0.5	Colon Pool	5.4
Ovarian ca. OVCAR-5	7.2	Small Intestine Pool	14.4
Ovarian ca. IGROV-1	12.5	Stomach Pool	6.0
Ovarian ca. OVCAR-8	6.5	Bone Marrow Pool	4.1
Ovary	18.8	Fetal Heart	12.7
Breast ca. MCF-7	0.2	Heart Pool	14.3
Breast ca. MDA-MB-231	5.6	Lymph Node Pool	7.4
Breast ca. BT 549	1.0	Fetal Skeletal Muscle	14.8
Breast ca. T47D	9.0	Skeletal Muscle Pool	43.5
Breast ca. MDA-N	0.6	Spleen Pool	16.7
Breast Pool	5.6	Thymus Pool	8.5

Trachea	12.4	CNS cancer (glio/astro) U87-MG	7.5
Lung	2.1	CNS cancer (glio/astro) U-118-MG	58.6
Fetal Lung	83.5	CNS cancer (neuro;met) SK-N-AS	23.7
Lung ca. NCI-N417	3.4	CNS cancer (astro) SF-539	1.9
Lung ca. LX-1	2.6	CNS cancer (astro) SNB-75	1.5
Lung ca. NCI-H146	20.9	CNS cancer (glio) SNB-19	12.2
Lung ca. SHP-77	20.9	CNS cancer (glio) SF-295	4.8
Lung ca. A549	37.9	Brain (Amygdala) Pool	28.9
Lung ca. NCI-H526	10.2	Brain (cerebellum)	59.9
Lung ca. NCI-H23	16.2	Brain (fetal)	34.2
Lung ca. NCI-H460	5.2	Brain (Hippocampus) Pool	40.6
Lung ca. HOP-62	3.1	Cerebral Cortex Pool	62.9
Lung ca. NCI-H522	38.2	Brain (Substantia nigra) Pool	39.0
Liver	0.9	Brain (Thalamus) Pool	56.6
Fetal Liver	2.2	Brain (whole)	58.2
Liver ca. HepG2	14.0	Spinal Cord Pool	58.2
Kidney Pool	15.9	Adrenal Gland	12.1
Fetal Kidney	21.6	Pituitary gland Pool	6.7
Renal ca. 786-0	6.6	Salivary Gland	4.8
Renal ca. A498	3.7	Thyroid (female)	13.1
Renal ca. ACHN	19.2	Pancreatic ca. CAPAN2	0.1
Renal ca. UO-31	8.2	Pancreas Pool	10.5

Table UD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3258, Run 164537289	Tissue Name	Rel. Exp.(%) Ag3258, Run 164537289
Secondary Th1 act	0.3	HUVEC IL-1beta	3.2
Secondary Th2 act	3.8	HUVEC IFN gamma	6.5
Secondary Tr1 act	0.3	HUVEC TNF alpha + IFN gamma	4.2
Secondary Th1 rest	0.2	HUVEC TNF alpha + IL4	5.2
Secondary Th2 rest	0.0	HUVEC IL-11	3.4
Secondary Tr1 rest	0.0	Lung Microvascular EC none	4.4
Primary Th1 act	2.4	Lung Microvascular EC TNFalpha + IL-1beta	1.8
Primary Th2 act	0.0	Microvascular Dermal EC none	8.5
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	4.9
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	14.9
Primary Th2 rest	0.2	Small airway epithelium none	2.1
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	19.3
CD45RA CD4 lymphocyte act	3.0	Coronary artery SMC rest	13.3
CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	9.4
CD8 lymphocyte act	0.0	Astrocytes rest	21.9
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	3.5
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.3

2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	24.5
LAK cells rest	1.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	6.2
LAK cells IL-2	0.4	Liver cirrhosis	1.0
LAK cells IL-2+IL-12	0.0	Lupus kidney	3.9
LAK cells IL-2+IFN gamma	3.1	NCI-H292 none	78.5
LAK cells IL-2+ IL-18	0.7	NCI-H292 IL-4	100.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	87.1
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	53.2
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	37.6
Two Way MLR 5 day	0.0	HPAEC none	1.3
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	2.9
PBMC rest	0.0	Lung fibroblast none	16.5
PBMC PWM	2.1	Lung fibroblast TNF alpha + IL-1 beta	14.0
PBMC PHA-L	0.3	Lung fibroblast IL-4	21.8
Ramos (B cell) none	13.1	Lung fibroblast IL-9	17.4
Ramos (B cell) ionomycin	42.3	Lung fibroblast IL-13	13.6
B lymphocytes PWM	4.2	Lung fibroblast IFN gamma	20.6
B lymphocytes CD40L and IL-4	0.4	Dermal fibroblast CCD1070 rest	20.6
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	12.9
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	20.3
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	13.3
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	33.7
Dendritic cells anti-CD40	0.0	IBD Colitis 2	1.6
Monocytes rest	0.0	IBD Crohn's	9.8
Monocytes LPS	0.0	Colon	52.9
Macrophages rest	0.0	Lung	17.3
Macrophages LPS	0.3	Thymus	13.4
HUVEC none	5.9	Kidney	29.3
HUVEC starved	10.3		

CNS_neurodegeneration_v1.0 Summary: Ag3258 This panel confirms the expression of this gene at low levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 5 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3258 This gene is expressed at high to moderate levels in the majority of samples on this panel. In particular, high levels of CG57503-01 gene expression are seen in all regions of the central nervous system examined, 10 including in amygdala, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as

Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

The expression of this gene in metabolic tissues such as pancreas, thyroid, pituitary gland, adrenal gland, skeletal muscle, heart, adipose, and liver suggests that modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

In addition, there is substantial expression of this gene associated with several cancer cell lines, particularly melanoma and lung cancer cell lines. Therefore, therapeutic modulation of the activity of this gene or its protein product, through the use of small molecule drugs, protein therapeutics or antibodies, might be beneficial in the treatment of melanoma and lung cancer.

Interestingly, this gene is expressed at much higher levels in fetal lung (CT=25.6) than in adult lung (CT=31.0). This observation suggests that expression of this gene can be used to distinguish fetal from adult lung tissue.

Panel 4D Summary: Ag3258 Expression of the CG57503-01 gene is highest in the lung-derived mucoepidermoid cell line NCI-H292 (CT = 28.1). Thus, therapeutic modulation of the activity of this gene, using small molecule drugs, antibodies or protein therapeutics, may be of use in the treatment of asthma and emphysema. Low to moderate expression of this gene is also seen in a number of fibroblast and epithelial cell lines.

The CG57503-01 gene encodes a protein with homology to MEGF7 and is a Type I membrane protein with 7 LDL-R type A domains, 19 LDL-R type B domains, 11 EGF domains, and a cytoplasmic tail of >100 residues. This protein may act as a cell surface receptor for an uncharacterized ligand and play a role in Ca⁺⁺-dependent functions, as is the case for other proteins with multiple EGF domains. Expression of the CG57503-01 gene at moderate levels in the brain, in lung and skin fibroblasts, and selectively in the pulmonary epidermoid carcinoma cell line NCI-H292, suggests that therapeutic antibodies and small molecule antagonists that block its function may be useful in reduction or elimination of the symptoms of asthma, emphysema, or psoriasis.

NOV27

Expression of gene NOV27/CG57658-01 was assessed using the primer-probe set Ag3299, described in Table VA. Results of the RTQ-PCR runs are shown in Tables VB, VC and VD.

Table VA. Probe Name Ag3299

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-cttctctcttccaggaaagc-3'	21	14	328
Probe	TET-5'-tctggctcgtcctcacgatgctg-3'-TAMRA	23	35	329
Reverse	5'-tctgtctcgtcctggtaga-3'	19	95	340

Table VB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3299, Run 210063511	Tissue Name	Rel. Exp.(%) Ag3299, Run 210063511
AD 1 Hippo	0.0	Control (Path) 3 Temporal Ctx	6.3
AD 2 Hippo	12.0	Control (Path) 4 Temporal Ctx	79.6
AD 3 Hippo	0.0	AD 1 Occipital Ctx	21.5
AD 4 Hippo	3.3	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	78.5	AD 3 Occipital Ctx	4.1
AD 6 Hippo	13.9	AD 4 Occipital Ctx	23.3
Control 2 Hippo	22.8	AD 5 Occipital Ctx	8.0
Control 4 Hippo	0.0	AD 6 Occipital Ctx	44.4
Control (Path) 3 Hippo	5.4	Control 1 Occipital Ctx	0.0
AD 1 Temporal Ctx	10.2	Control 2 Occipital Ctx	89.5
AD 2 Temporal Ctx	51.8	Control 3 Occipital Ctx	16.8
AD 3 Temporal Ctx	12.9	Control 4 Occipital Ctx	0.0
AD 4 Temporal Ctx	22.1	Control (Path) 1 Occipital Ctx	66.4
AD 5 Inf Temporal Ctx	72.7	Control (Path) 2 Occipital Ctx	20.4
AD 5 SupTemporal Ctx	6.0	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	32.3	Control (Path) 4 Occipital Ctx	21.5
AD 6 Sup Temporal Ctx	32.8	Control 1 Parietal Ctx	10.2
Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	35.1
Control 2 Temporal Ctx	37.4	Control 3 Parietal Ctx	21.5
Control 3 Temporal Ctx	20.4	Control (Path) 1 Parietal Ctx	100.0
Control 4 Temporal Ctx	3.2	Control (Path) 2 Parietal Ctx	22.2
Control (Path) 1 Temporal Ctx	94.0	Control (Path) 3 Parietal Ctx	0.0
Control (Path) 2 Temporal Ctx	45.7	Control (Path) 4 Parietal Ctx	66.9

Table VC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3299, Run 215620706	Tissue Name	Rel. Exp.(%) Ag3299, Run 215620706
Adipose	2.1	Renal ca. TK-10	2.8
Melanoma* Hs688(A).T	4.4	Bladder	0.0
Melanoma* Hs688(B).T	12.1	Gastric ca. (liver met.) NCI-N87	7.3
Melanoma* M14	0.0	Gastric ca. KATO III	1.1
Melanoma* LOXIMVI	4.1	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	0.0
Squamous cell carcinoma SCC-4	0.0	Colon ca.* (SW480 met) SW620	0.0

Testis Pool	8.5	Colon ca. HT29	0.0
Prostate ca.* (bone met) PC-3	100.0	Colon ca. HCT-116	4.4
Prostate Pool	6.7	Colon ca. CaCo-2	0.0
Placenta	0.0	Colon cancer tissue	4.0
Uterus Pool	0.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	6.7	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	6.0	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	0.0	Colon Pool	7.6
Ovarian ca. OVCAR-5	2.0	Small Intestine Pool	9.7
Ovarian ca. IGROV-1	0.0	Stomach Pool	17.0
Ovarian ca. OVCAR-8	0.0	Bone Marrow Pool	2.8
Ovary	0.0	Fetal Heart	2.1
Breast ca. MCF-7	0.0	Heart Pool	0.0
Breast ca. MDA-MB-231	8.4	Lymph Node Pool	7.0
Breast ca. BT 549	6.8	Fetal Skeletal Muscle	2.2
Breast ca. T47D	2.5	Skeletal Muscle Pool	0.0
Breast ca. MDA-N	0.0	Spleen Pool	4.1
Breast Pool	6.1	Thymus Pool	12.9
Trachea	0.0	CNS cancer (glio/astro) U87-MG	2.1
Lung	1.8	CNS cancer (glio/astro) U-118-MG	3.6
Fetal Lung	6.8	CNS cancer (neuro;met) SK-N-AS	0.0
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	0.0	CNS cancer (astro) SNB-75	2.0
Lung ca. NCI-H146	13.8	CNS cancer (glio) SNB-19	1.3
Lung ca. SHP-77	3.9	CNS cancer (glio) SF-295	0.0
Lung ca. A549	0.0	Brain (Amygdala) Pool	21.2
Lung ca. NCI-H526	0.0	Brain (cerebellum)	5.5
Lung ca. NCI-H23	47.0	Brain (fetal)	14.3
Lung ca. NCI-H460	10.2	Brain (Hippocampus) Pool	13.9
Lung ca. HOP-62	2.2	Cerebral Cortex Pool	38.7
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	20.9
Liver	0.0	Brain (Thalamus) Pool	33.4
Fetal Liver	0.0	Brain (whole)	36.1
Liver ca. HepG2	0.0	Spinal Cord Pool	4.2
Kidney Pool	9.8	Adrenal Gland	3.8
Fetal Kidney	17.6	Pituitary gland Pool	4.1
Renal ca. 786-0	2.6	Salivary Gland	0.0
Renal ca. A498	0.0	Thyroid (female)	0.0
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	3.0
Renal ca. UO-31	0.0	Pancreas Pool	2.1

Table VD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3299, Run 164682522	Tissue Name	Rel. Exp.(%) Ag3299, Run 164682522
Secondary Th1 act	2.4	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	7.2	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	11.2
Secondary Tr1 rest	0.0	Lung Microvascular EC none	25.5

Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	18.9
Primary Th2 act	0.0	Microvascular Dermal EC none	9.9
Primary Tr1 act	8.5	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	12.5
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	19.8
CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	9.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	66.4
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	10.2
LAK cells IL-2+ IL-18	13.3	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	9.7
NK Cells IL-2 rest	12.5	NCI-H292 IL-13	19.6
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	8.6	HPAEC none	9.2
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	11.3	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	9.7
B lymphocytes PWM	23.5	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	19.5
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	7.7
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	11.2	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	100.0
Macrophages rest	0.0	Lung	41.2
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	5.9	Kidney	9.2
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag3299 This panel confirms the expression of this gene at low levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3299 The CG57658-01 gene is expressed at highest levels in prostate cancer cell line PC-3 (CT=30.5). Interestingly, this gene is expressed at much lower levels in the normal prostate. Therefore, therapeutic modulation of the activity of this gene, using small molecule drugs, antibodies or protein therapeutics, may be of benefit in the treatment of prostate cancer.

This gene is also expressed at low levels in all regions of the brain examined, including amygdala, cerebral cortex, cerebellum, substantia nigra, thalamus and hippocampus. The CG57658-01 gene encodes a protein that is a variant of the human CONNEXIN40.1 gene. Cell-specific expression of connexins in the central nervous system has been shown to regulate gap junctional coupling between glial cells and neurons (ref. 1). Therefore, modulation of the activity of this gene or its protein product may be useful in the treatment of inherited demyelinating neuropathies or other neurological diseases.

References:

1. Rash JE, Yasumura T, Dudek FE, Nagy JJ. Cell-specific expression of connexins and evidence of restricted gap junctional coupling between glial cells and between neurons. *J Neurosci* 2001 Mar 15;21(6):1983-2000

The transmembrane connexin proteins of gap junctions link extracellularly to form channels for cell-to-cell exchange of ions and small molecules. Two primary hypotheses of gap junction coupling in the CNS are the following: (1) generalized coupling occurs between neurons and glia, with some connexins expressed in both neurons and glia, and (2) intercellular junctional coupling is restricted to specific coupling partners, with different connexins expressed in each cell type. There is consensus that gap junctions link neurons to neurons and astrocytes to oligodendrocytes, ependymocytes, and other astrocytes. However, unresolved are the existence and degree to which gap junctions occur between oligodendrocytes, between oligodendrocytes and neurons, and between astrocytes and neurons. Using light microscopic immunocytochemistry and freeze-fracture replica immunogold labeling of adult rat CNS, we investigated whether four of the best-characterized CNS connexins are each present in one or more cell types, whether oligodendrocytes also share gap junctions with other

oligodendrocytes or with neurons, and whether astrocytes share gap junctions with neurons. Connexin32 (Cx32) was found only in gap junctions of oligodendrocyte plasma membranes, Cx30 and Cx43 were found only in astrocyte membranes, and Cx36 was only in neurons. Oligodendrocytes shared intercellular gap junctions only with astrocytes, with each oligodendrocyte isolated from other oligodendrocytes except via astrocyte intermediaries. Finally, neurons shared gap junctions only with other neurons and not with glial cells. Thus, the different cell types of the CNS express different connexins, which define separate pathways for neuronal versus glial gap junctional communication.

PMID: 11245683

- 10 **Panel 4D Summary:** [Ag3299](#) The CG57658-01 gene, which encodes a variant of the human CONNEXIN40.1 gene, is expressed at highest levels in the colon (CT = 30) and appears to be down-regulated in colon tissue isolated from Crohn's and colitis patients (CT = 40). Connexin is expressed in GAP junctions in gastrointestinal muscle (ref. 1). Thus, the expression of the transcript or the protein it encodes could be used to detect normal colon tissue. Furthermore, therapeutic modulation of the activity of this gene or its protein product could be useful in the treatment of inflammatory bowel disease.

References:

1. Wang YF, Daniel EE. Gap junctions in gastrointestinal muscle contain multiple connexins. *Am J Physiol Gastrointest Liver Physiol* 2001 Aug;281(2):G533-43.
- 20 In the canine gastrointestinal tract, the roles that gap junctions play in pacemaking and neurotransmission are unclear. Using antibodies to connexin (Cx)43, Cx45, and Cx40, we determined the distribution of these connexins. Cx43 was present in all locations where structural gap junctions occur. Cx40 was also widely distributed in the circular muscle of the lower esophageal sphincter (LES), stomach, and ileum. Cx45 was sparsely distributed in circular muscle of the LES. In the interstitial cells of Cajal (ICC) networks of myenteric plexus, in the deep muscular and submuscular plexuses, sparse Cx45 and Cx40 immunoreactivity was present. In colon, immunoreactivity was found only in the myenteric and submuscular plexus and nearby circular muscle cells. No immunoreactivity was found in sites lacking structural gap junctions (longitudinal muscle, inner circular muscle of the intestine, and most circular muscle of the colon). Studies of colocalization of connexins suggested that in the ICC networks, some colocalization of Cx43 with Cx40 and/or Cx45 occurred. Thus gap junctions in canine intestine may be heterotypic or heteromeric and have
- 30

different conductance properties in different regions based on different connexin compositions.

PMID: 11447034

NOV28

- 5 Expression of gene NOV28/CG57662-01 was assessed using the primer-probe set Ag3300, described in Table WA. Results of the RTQ-PCR runs are shown in Tables WB, WC and WD.

Table WA. Probe Name Ag3300

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-aaagatgctgaaggagtgaaga-3'	22	914	341
Probe	TET-5'-ccatcccctaatacgcaggatggta-3'-TAMRA	26	941	342
Reverse	5'-tctgagagaggagtttctcaa-3'	22	992	343

Table WB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3300, Run 210063573	Tissue Name	Rel. Exp.(%) Ag3300, Run 210063573
AD 1 Hippo	0.0	Control (Path) 3 Temporal Ctx	0.0
AD 2 Hippo	0.0	Control (Path) 4 Temporal Ctx	0.0
AD 3 Hippo	0.0	AD 1 Occipital Ctx	0.0
AD 4 Hippo	0.0	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	0.0	AD 3 Occipital Ctx	0.0
AD 6 Hippo	16.6	AD 4 Occipital Ctx	0.0
Control 2 Hippo	7.1	AD 5 Occipital Ctx	0.0
Control 4 Hippo	0.0	AD 6 Occipital Ctx	0.0
Control (Path) 3 Hippo	0.0	Control 1 Occipital Ctx	0.0
AD 1 Temporal Ctx	0.0	Control 2 Occipital Ctx	0.0
AD 2 Temporal Ctx	0.0	Control 3 Occipital Ctx	38.4
AD 3 Temporal Ctx	0.0	Control 4 Occipital Ctx	0.0
AD 4 Temporal Ctx	0.0	Control (Path) 1 Occipital Ctx	100.0
AD 5 Inf Temporal Ctx	42.6	Control (Path) 2 Occipital Ctx	0.0
AD 5 Sup Temporal Ctx	0.0	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	0.0	Control (Path) 4 Occipital Ctx	0.0
AD 6 Sup Temporal Ctx	0.0	Control 1 Parietal Ctx	39.8
Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	0.0
Control 2 Temporal Ctx	0.0	Control 3 Parietal Ctx	0.0
Control 3 Temporal Ctx	0.0	Control (Path) 1 Parietal Ctx	0.0
Control 3 Temporal Ctx	0.0	Control (Path) 2 Parietal Ctx	0.0
Control (Path) 1 Temporal Ctx	57.0	Control (Path) 3 Parietal Ctx	0.0
Control (Path) 2 Temporal Ctx	41.8	Control (Path) 4 Parietal Ctx	0.0

Table WC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3300, Run 215669620	Rel. Exp.(%) Ag3300, Run 217235346	Tissue Name	Rel. Exp.(%) Ag3300, Run 215669620	Rel. Exp.(%) Ag3300, Run 217235346
Adipose	0.0	0.0	Renal ca. TK-10	5.5	10.4
Melanoma* Hs688(A).T	0.0	0.0	Bladder	0.0	0.0
Melanoma* Hs688(B).T	0.0	0.0	Gastric ca. (liver met.) NCI-N87	0.0	0.0
Melanoma* M14	0.0	0.0	Gastric ca. KATO III	0.0	0.0
Melanoma* LOXIMVI	0.0	0.0	Colon ca. SW-948	0.0	10.2
Melanoma* SK- MEL-5	0.0	0.0	Colon ca. SW480	0.0	0.0
Squamous cell carcinoma SCC-4	0.0	0.0	Colon ca.* (SW480 met) SW620	0.0	0.0
Testis Pool	4.1	5.6	Colon ca. HT29	0.0	0.0
Prostate ca.* (bone met) PC-3	0.0	7.1	Colon ca. HCT-116	0.0	0.0
Prostate Pool	13.1	29.7	Colon ca. CaCo-2	0.0	17.2
Placenta	0.0	0.0	Colon cancer tissue	8.7	18.4
Uterus Pool	0.0	0.0	Colon ca. SW1116	0.0	0.0
Ovarian ca. OVCAR-3	0.0	0.0	Colon ca. Colo-205	0.0	0.0
Ovarian ca. SK- OV-3	0.0	0.0	Colon ca. SW-48	0.0	0.0
Ovarian ca. OVCAR-4	0.0	0.0	Colon Pool	0.0	0.0
Ovarian ca. OVCAR-5	19.1	6.7	Small Intestine Pool	0.0	5.9
Ovarian ca. IGROV-1	0.0	0.0	Stomach Pool	0.0	0.0
Ovarian ca. OVCAR-8	0.0	0.0	Bone Marrow Pool	0.0	0.0
Ovary	0.0	0.0	Fetal Heart	0.0	0.0
Breast ca. MCF-7	7.4	0.0	Heart Pool	0.0	0.0
Breast ca. MDA- MB-231	0.0	0.0	Lymph Node Pool	0.0	0.0
Breast ca. BT 549	0.0	0.0	Fetal Skeletal Muscle	0.0	0.0
Breast ca. T47D	43.5	63.7	Skeletal Muscle Pool	0.0	0.0
Breast ca. MDA- N	0.0	0.0	Spleen Pool	0.0	0.0
Breast Pool	0.0	0.0	Thymus Pool	0.0	5.3
Trachea	4.4	0.0	CNS cancer (glio/astro) U87-MG	0.0	0.0
Lung	0.0	0.0	CNS cancer (glio/astro) U-118- MG	5.4	5.4
Fetal Lung	3.5	0.0	CNS cancer (neuro;met) SK-N- AS	0.0	0.0
Lung ca. NCI- N417	0.0	0.0	CNS cancer (astro) SF-539	0.0	0.0
Lung ca. LX-1	0.0	0.0	CNS cancer (astro) SNB-75	0.0	0.0
Lung ca. NCI- H146	16.0	0.0	CNS cancer (glio) SNB-19	0.0	0.0
Lung ca. SHP-77	0.0	0.0	CNS cancer (glio)	0.0	0.0

			SF-295		
Lung ca. A549	0.0	0.0	Brain (Amygdala) Pool	6.3	0.0
Lung ca. NCI-H526	100.0	100.0	Brain (cerebellum)	0.0	6.8
Lung ca. NCI-H23	88.3	0.0	Brain (fetal)	7.9	13.9
Lung ca. NCI-H460	34.4	0.0	Brain (Hippocampus) Pool	0.0	0.0
Lung ca. HOP-62	0.0	0.0	Cerebral Cortex Pool	0.0	0.0
Lung ca. NCI-H522	0.0	0.0	Brain (Substantia nigra) Pool	0.0	0.0
Liver	0.0	8.2	Brain (Thalamus) Pool	4.9	0.0
Fetal Liver	15.5	16.5	Brain (whole)	10.2	0.0
Liver ca. HepG2	8.0	7.1	Spinal Cord Pool	0.0	0.0
Kidney Pool	0.0	12.7	Adrenal Gland	0.0	0.0
Fetal Kidney	0.0	7.6	Pituitary gland Pool	0.0	0.0
Renal ca. 786-0	0.0	0.0	Salivary Gland	19.6	14.3
Renal ca. A498	39.8	0.0	Thyroid (female)	0.0	0.0
Renal ca. ACHN	0.0	0.0	Pancreatic ca. CAPAN2	0.0	0.0
Renal ca. UO-31	0.0	0.0	Pancreas Pool	0.0	0.0

Table WD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3300, Run 164682539	Tissue Name	Rel. Exp.(%) Ag3300, Run 164682539
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	12.7	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0

LAK cells IL-2	0.0	Liver cirrhosis	74.2
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	31.4	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	16.5	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	24.8
Macrophages rest	0.0	Lung	37.1
Macrophages LPS	0.0	Thymus	100.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag3300 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3300 Two experiments using the same probe/primer set on this panel yielded similar results. Significant expression of the CG57662-01 gene is seen only in breast, renal, and lung cancer cell lines. Therefore, expression of this gene can be used to differentiate these lines from from the other samples on this panel. Furthermore, therapeutic modulation of the activity of this gene or its protein product, using small molecule drugs, antibodies or protein therapeutics, may be of use in the treatment of breast, renal, and lung cancer.

Panel 4D Summary: Ag3300 The CG57662-01 gene is expressed at significant levels only in the thymus (CT = 34.6). The putative connexin encoded for by this gene could therefore play an important role in T cell development. Small molecule therapeutics, or antibody therapeutics designed against the GPCR encoded for by this gene could be utilized to

modulate immune function (T cell development) and be important for organ transplant, AIDS treatment or post chemotherapy immune reconstitution.

References:

1. Evans WH, Boitano S. Connexin mimetic peptides: specific inhibitors of gap-junctional intercellular communication. Biochem Soc Trans. 2001 Aug;29(Pt 4):606-12.

Intercellular co-operation is a fundamental and widespread feature in tissues and organs. An important mechanism ensuring multicellular homoeostasis involves signalling between cells via gap junctions that directly connect the cytosolic contents of adjacent cells. Cell proliferation and intercellular communication across gap junctions are closely linked, and a number of pathologies in which communication is disrupted are known where connexins, the gap-junctional proteins, are modified. The proteins of gap junctions thus emerge as therapeutic targets inviting the development and exploitation of chemical tools and drugs that specifically influence intercellular communication. Connexin mimetic peptides that correspond to short specific sequences in the two extracellular loops of connexins are a class of benign, specific and reversible inhibitors of gap-junctional communication that have been studied recently in a broad range of cells, tissues and organs. This review summarizes the properties and uses of these short synthetic peptides, and compares their probable mechanism of action with those of a wide range of other less specific traditional gap-junction inhibitors.

NOV29

Expression of NOV29/CG57664-01 was assessed using the primer-probe sets Ag3301 and Ag3417, described in Tables XA and XB. Results of the RTQ-PCR runs are shown in Tables XC, XD and XE.

Table XA. Probe Name Ag3301

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ctacgatggcaaggattacac-3'	22	554	344
Probe	TET-5'-ctgaacgaggacctgccctcctg-3'-TAMRA	23	579	345
Reverse	5'-cacttgctgtgggagatctg-3'	20	624	346

Table XB. Probe Name Ag3417

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-cgcagattaccgagtgac-3'	20	400	347
Probe	TET-5'-gacctgctccgctattacaaccaga-3'-TAMRA	26	425	348
Reverse	5'-ctggatggtgtgagaaccac-3'	20	460	349

Table XC. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3301, Run 210063574	Tissue Name	Rel. Exp.(%) Ag3301, Run 210063574
AD 1 Hippo	34.4	Control (Path) 3 Temporal	8.8

		Ctx	
AD 2 Hippo	48.0	Control (Path) 4 Temporal Ctx	71.2
AD 3 Hippo	3.8	AD 1 Occipital Ctx	46.0
AD 4 Hippo	15.6	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	77.4	AD 3 Occipital Ctx	8.3
AD 6 Hippo	100.0	AD 4 Occipital Ctx	36.1
Control 2 Hippo	29.1	AD 5 Occipital Ctx	33.4
Control 4 Hippo	33.0	AD 6 Occipital Ctx	25.3
Control (Path) 3 Hippo	4.6	Control 1 Occipital Ctx	10.6
AD 1 Temporal Ctx	33.4	Control 2 Occipital Ctx	41.5
AD 2 Temporal Ctx	36.6	Control 3 Occipital Ctx	27.2
AD 3 Temporal Ctx	7.9	Control 4 Occipital Ctx	10.7
AD 4 Temporal Ctx	69.3	Control (Path) 1 Occipital Ctx	94.6
AD 5 Inf Temporal Ctx	39.5	Control (Path) 2 Occipital Ctx	26.8
AD 5 Sup Temporal Ctx	36.9	Control (Path) 3 Occipital Ctx	4.1
AD 6 Inf Temporal Ctx	94.0	Control (Path) 4 Occipital Ctx	45.4
AD 6 Sup Temporal Ctx	96.6	Control 1 Parietal Ctx	21.0
Control 1 Temporal Ctx	15.7	Control 2 Parietal Ctx	36.1
Control 2 Temporal Ctx	37.6	Control 3 Parietal Ctx	20.6
Control 3 Temporal Ctx	14.7	Control (Path) 1 Parietal Ctx	71.7
Control 4 Temporal Ctx	20.0	Control (Path) 2 Parietal Ctx	43.2
Control (Path) 1 Temporal Ctx	85.9	Control (Path) 3 Parietal Ctx	5.4
Control (Path) 2 Temporal Ctx	52.9	Control (Path) 4 Parietal Ctx	88.9

Table XD. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3301, Run 215670031	Rel. Exp.(%) Ag3301, Run 217235352	Tissue Name	Rel. Exp.(%) Ag3301, Run 215670031	Rel. Exp.(%) Ag3301, Run 217235352
Adipose	7.4	7.9	Renal ca. TK-10	1.6	0.9
Melanoma* Hs688(A).T	2.0	1.8	Bladder	18.3	20.7
Melanoma* Hs688(B).T	1.3	1.8	Gastric ca. (liver met.) NCI-N87	57.0	52.5
Melanoma* M14	0.2	0.4	Gastric ca. KATO III	25.5	27.7
Melanoma* LOXIMVI	5.9	4.0	Colon ca. SW-948	4.6	4.8
Melanoma* SK- MEL-5	3.3	4.0	Colon ca. SW480	7.9	6.9
Squamous cell carcinoma SCC-4	1.4	1.4	Colon ca.* (SW480 met) SW620	3.6	3.1
Testis Pool	2.3	1.5	Colon ca. HT29	0.0	0.0
Prostate ca.* (bone met) PC-3	5.0	4.2	Colon ca. HCT-116	3.2	3.4
Prostate Pool	4.5	4.6	Colon ca. CaCo-2	0.4	0.5
Placenta	4.4	4.4	Colon cancer tissue	87.7	100.0
Uterus Pool	1.8	1.7	Colon ca. SW1116	2.3	3.5
Ovarian ca. OVCAR-3	8.6	8.4	Colon ca. Colo-205	8.8	6.7

Ovarian ca. SK-OV-3	2.5	4.3	Colon ca. SW-48	25.0	16.8
Ovarian ca. OVCAR-4	8.8	9.1	Colon Pool	6.8	7.5
Ovarian ca. OVCAR-5	32.5	20.6	Small Intestine Pool	6.8	6.7
Ovarian ca. IGROV-1	6.2	4.2	Stomach Pool	5.3	7.6
Ovarian ca. OVCAR-8	24.8	30.8	Bone Marrow Pool	1.9	1.7
Ovary	9.1	7.7	Fetal Heart	1.4	0.9
Breast ca. MCF-7	0.4	0.3	Heart Pool	2.9	4.4
Breast ca. MDA-MB-231	100.0	73.2	Lymph Node Pool	8.6	9.8
Breast ca. BT 549	8.5	9.3	Fetal Skeletal Muscle	0.6	0.4
Breast ca. T47D	86.5	93.3	Skeletal Muscle Pool	3.5	4.1
Breast ca. MDA-N	0.3	0.3	Spleen Pool	24.5	31.9
Breast Pool	7.5	6.2	Thymus Pool	13.2	11.7
Trachea	15.5	13.6	CNS cancer (glio/astro) U87-MG	0.1	0.2
Lung	0.9	1.1	CNS cancer (glio/astro) U-118-MG	8.9	10.7
Fetal Lung	8.1	9.2	CNS cancer (neuro;met) SK-N-AS	5.8	4.9
Lung ca. NCI-N417	0.1	0.2	CNS cancer (astro) SF-539	14.4	18.3
Lung ca. LX-1	6.0	6.8	CNS cancer (astro) SNB-75	21.5	34.4
Lung ca. NCI-H146	0.8	0.4	CNS cancer (glio) SNB-19	6.3	5.0
Lung ca. SHP-77	0.2	0.3	CNS cancer (glio) SF-295	22.4	17.9
Lung ca. A549	4.4	3.8	Brain (Amygdala) Pool	4.5	3.5
Lung ca. NCI-H526	15.3	12.8	Brain (cerebellum)	7.3	5.4
Lung ca. NCI-H23	15.1	9.4	Brain (fetal)	4.9	5.6
Lung ca. NCI-H460	10.7	9.8	Brain (Hippocampus) Pool	4.1	3.6
Lung ca. HOP-62	20.6	18.3	Cerebral Cortex Pool	4.2	3.8
Lung ca. NCI-H522	2.4	1.3	Brain (Substantia nigra) Pool	6.6	6.3
Liver	1.9	1.5	Brain (Thalamus) Pool	4.9	6.0
Fetal Liver	2.0	1.8	Brain (whole)	3.8	4.7
Liver ca. HepG2	1.2	1.2	Spinal Cord Pool	3.0	3.7
Kidney Pool	15.0	16.7	Adrenal Gland	7.3	7.9
Fetal Kidney	2.6	2.6	Pituitary gland Pool	2.7	2.3
Renal ca. 786-0	6.4	5.6	Salivary Gland	4.0	3.6
Renal ca. A498	11.7	10.6	Thyroid (female)	4.2	4.0
Renal ca. ACHN	4.2	2.6	Pancreatic ca. CAPAN2	13.6	9.6
Renal ca. UO-31	7.9	4.7	Pancreas Pool	11.9	13.6

Table XE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3301, Run 164682541	Rel. Exp.(%) Ag3417, Run 166453854	Tissue Name	Rel. Exp.(%) Ag3301, Run 164682541	Rel. Exp.(%) Ag3417, Run 166453854
Secondary Th1 act	13.6	0.0	HUVEC IL-1beta	0.2	0.0
Secondary Th2 act	44.4	0.0	HUVEC IFN gamma	5.9	100.0
Secondary Tr1 act	33.9	0.0	HUVEC TNF alpha + IFN gamma	0.4	0.0
Secondary Th1 rest	31.0	0.0	HUVEC TNF alpha + IL4	0.2	0.0
Secondary Th2 rest	22.4	0.0	HUVEC IL-11	1.9	0.0
Secondary Tr1 rest	34.9	0.0	Lung Microvascular EC none	8.5	0.0
Primary Th1 act	21.5	0.0	Lung Microvascular EC TNFalpha + IL-1beta	13.4	0.0
Primary Th2 act	22.5	0.0	Microvascular Dermal EC none	6.0	0.0
Primary Tr1 act	33.9	0.0	Microvascular Dermal EC TNFalpha + IL- 1beta	22.5	0.0
Primary Th1 rest	37.4	0.0	Bronchial epithelium TNFalpha + IL1beta	16.8	0.0
Primary Th2 rest	0.0	0.0	Small airway epithelium none	0.0	0.0
Primary Tr1 rest	17.2	0.0	Small airway epithelium TNFalpha + IL-1beta	0.7	0.0
CD45RA CD4 lymphocyte act	10.6	0.0	Coronary artery SMC rest	1.1	0.0
CD45RO CD4 lymphocyte act	29.3	0.0	Coronary artery SMC TNFalpha + IL-1beta	0.3	0.0
CD8 lymphocyte act	29.3	0.0	Astrocytes rest	8.1	0.0
Secondary CD8 lymphocyte rest	48.3	0.0	Astrocytes TNFalpha + IL-1beta	7.0	0.0
Secondary CD8 lymphocyte act	2.4	0.0	KU-812 (Basophil) rest	0.8	0.0
CD4 lymphocyte none	13.6	0.0	KU-812 (Basophil) PMA/ionomycin	2.4	0.0
2ry Th1/Th2/Tr1_anti- CD95 CH11	17.3	0.0	CCD1106 (Keratinocytes) none	4.1	0.0
LAK cells rest	100.0	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	12.0	0.0
LAK cells IL-2	54.7	0.0	Liver cirrhosis	8.4	0.0
LAK cells IL-2+IL-12	49.7	0.0	Lupus kidney	0.4	0.0
LAK cells IL-2+IFN gamma	44.8	0.0	NCI-H292 none	2.3	0.0
LAK cells IL-2+ IL- 18	34.2	0.0	NCI-H292 IL-4	3.6	0.0
LAK cells PMA/ionomycin	80.1	0.0	NCI-H292 IL-9	2.6	0.0
NK Cells IL-2 rest	24.1	0.0	NCI-H292 IL-13	1.4	0.0
Two Way MLR 3 day	58.6	0.0	NCI-H292 IFN gamma	1.4	0.0
Two Way MLR 5 day	25.9	0.0	HPAEC none	6.0	0.0
Two Way MLR 7 day	6.6	0.0	HPAEC TNF alpha + IL-1 beta	23.7	0.0
PBMC rest	14.5	0.0	Lung fibroblast none	0.7	0.0
PBMC PWM	35.4	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.1	0.0
PBMC PHA-L	24.8	0.0	Lung fibroblast IL-4	0.5	0.0
Ramos (B cell) none	8.4	0.0	Lung fibroblast IL-9	0.4	0.0

Ramos (B cell) ionomycin	14.7	0.0	Lung fibroblast IL-13	0.5	0.0
B lymphocytes PWM	12.9	0.0	Lung fibroblast IFN gamma	1.5	0.0
B lymphocytes CD40L and IL-4	18.4	0.0	Dermal fibroblast CCD1070 rest	12.5	0.0
EOL-1 dbcAMP	0.8	0.0	Dermal fibroblast CCD1070 TNF alpha	8.2	0.0
EOL-1 dbcAMP PMA/ionomycin	0.3	0.0	Dermal fibroblast CCD1070 IL-1 beta	6.5	0.0
Dendritic cells none	59.0	0.0	Dermal fibroblast IFN gamma	34.6	0.0
Dendritic cells LPS	10.8	0.0	Dermal fibroblast IL-4	9.7	0.0
Dendritic cells anti- CD40	16.8	0.0	IBD Colitis 2	1.2	0.0
Monocytes rest	36.1	0.0	IBD Crohn's	0.2	0.0
Monocytes LPS	30.1	0.0	Colon	27.2	0.0
Macrophages rest	17.3	0.0	Lung	6.1	0.0
Macrophages LPS	57.4	0.0	Thymus	8.4	0.0
HUVEC none	0.2	0.0	Kidney	33.7	0.0
HUVEC starved	0.4	0.0			

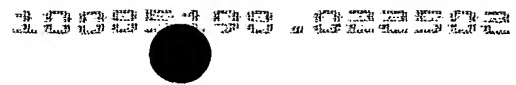
CNS_neurodegeneration_v1.0 Summary: Ag3301 This panel confirms the expression of this gene at low to moderate levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders. Ag3417 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3301 Results from two experiments with using the same probe/primer set yielded results that are in excellent agreement.

10 Expression of the CG57664-01 gene is moderate to high across the majority of samples on this panel, with highest expression in a colon cancer tissue (CT = 26.8). This gene appears to be more highly expressed in CNS, colon, gastric, renal, lung, ovarian, breast, and melanoma cancer cell lines when compared to normal tissues. The CG57664-01 gene encodes a protein with homology to MHC class 1 antigen. The major histocompatibility complex (MHC) class I

15 family of glycoproteins presents peptides for immunorecognition by cytotoxic T lymphocytes. Increased expression of this gene in cancer cell lines agrees with the results of other studies that found elevated levels of HLA class I antigen in tumors (ref. 1). Therefore, reduction in the expression or activity of this novel HLA class I antigen may make cancer cells sensitive to lysis by natural killer cells.

20 In addition, this gene is expressed at moderate levels in all regions of the central nervous system examined including amygdala, hippocampus, substantia nigra, cerebellum,



cerebral cortex, thalamus and spinal cord. Class I MHC molecules, known to be important for immune responses to antigen, are expressed also by neurons that undergo activity-dependent, long-term structural and synaptic modifications (ref. 2). Specific class I MHC mRNAs are expressed by distinct mosaics of neurons, reflecting a potential for diverse neuronal functions and suggesting an important role for these molecules in the activity-dependent remodeling and plasticity of connections in the developing and mature mammalian central nervous system.

Among tissues with metabolic or endocrine function, this gene is expressed at moderate levels in adrenal gland, thyroid, pituitary gland, pancreas, adipose, skeletal muscle, heart and liver. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

References:

1. Sette A, Chesnut R, Fikes J. HLA expression in cancer: implications for T cell-based immunotherapy. *Immunogenetics* 2001 May-Jun;53(4):255-63.

HLA class I expression is altered in a significant fraction of the tumor types reviewed here, reflecting either immune pressure or, simply, the accumulation of pathological changes and alterations. However, in all tumor types analyzed, a majority of the tumors express HLA class I. with a general tendency for the more severe alterations to be found in later-stage and less differentiated tumors. These results are encouraging for the development of specific immunotherapies, especially considering that (1) the relatively low sensitivity of immunohistochemical techniques might underestimate HLA expression in tumors, (2) class I expression can be induced in tumor cells as a result of local inflammation and lymphokine release, and (3) class I-negative cells would be predicted to be sensitive to lysis by natural killer cells.

PMID: 11491528

2. Huh GS, Boulanger LM, Du H, Riquelme PA, Brotz TM, Shatz CJ. Functional requirement for class I MHC in CNS development and plasticity. *Science* 2000 Dec 15;290(5499):2155-9

Class I major histocompatibility complex (class I MHC) molecules, known to be important for immune responses to antigen, are expressed also by neurons that undergo activity-dependent, long-term structural and synaptic modifications. Here, we show that in mice genetically deficient for cell surface class I MHC or for a class I MHC receptor component, CD3zeta, refinement of connections between retina and central targets during development is incomplete. In the hippocampus of adult mutants, N-methyl-D aspartate

receptor-dependent long-term potentiation (LTP) is enhanced, and long-term depression (LTD) is absent. Specific class I MHC messenger RNAs are expressed by distinct mosaics of neurons, reflecting a potential for diverse neuronal functions. These results demonstrate an important role for these molecules in the activity dependent remodeling and plasticity of connections in the developing and mature mammalian central nervous system (CNS).

PMID: 11118151

Panel 4D Summary: Ag3301 The CG57664-01 gene is moderately expressed in a number of samples on this panel, with highest expression in lymphokine-activated killer (LAK) cells (CT = 26-28), independent of stimulation. This observation suggests that modulation of the expression or activity of this gene may be useful in the treatment of intracellular bacterial or viral infections. This gene is also expressed at significant levels in T cells, B cells, dendritic cells, monocytes and macrophages.

The CG57664-01 gene encodes a protein with homology to MHC class I antigen. Major histocompatibility complex (MHC) class I molecules present antigenic peptides to CD8-positive T cells. The HLA class I gene family in humans consists of 6 members: polymorphic HLA-A, HLA-B, and HLA-C, and oligomorphic HLA-E, HLA-F, and HLA-G. HLA-A/B-alleles such as the CG57664-01 gene may have utility in genotyping criminals as well as in paternity disputes. These antigens are ubiquitously expressed on all nucleated human cells except neurons and trophoblasts, and participate in antigen presentation of viral antigens in the adaptive immune response.

Ag3417 Results from one experiment with the CG57664-01 gene are not included. The amp plot indicates that there were experimental difficulties with this run.

NOV30

Expression of NOV30/CG57666-01 was assessed using the primer-probe set Ag3302, described in Table YA.

Table YA. Probe Name Ag3302

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gtgatgtgcaggaagaactcat-3'	22	1056	350
Probe	TET-5'-ttgttctaccccaggcagcaacct-3'-TAMRA	26	1078	351
Reverse	5'-ttacaagccgtgagagacaca-3'	21	1118	352

CNS_neurodegeneration_v1.0 Summary: Ag3302 Expression of the CG57666-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3302 Expression of the CG57666-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag3302 Expression of the CG57666-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV31

5 Expression of NOV31/CG57668-01 was assessed using the primer-probe set Ag3303, described in Table ZA. Results of the RTQ-PCR runs are shown in Tables ZB, ZC and ZD.

Table ZA. Probe Name Ag3303

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ctacgacggcaaggattacat-3'	21	438	353
Probe	TET-5'-ctctgaacgaggacctgcgtcct-3'-TAMRA	24	461	354
Reverse	5'-gtgatctgagctgcatgtc-3'	20	496	355

Table ZB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3303, Run 210063655	Tissue Name	Rel. Exp.(%) Ag3303, Run 210063655
AD 1 Hippo	27.4	Control (Path) 3 Temporal Ctx	16.6
AD 2 Hippo	55.9	Control (Path) 4 Temporal Ctx	14.5
AD 3 Hippo	14.3	AD 1 Occipital Ctx	16.3
AD 4 Hippo	35.6	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	96.6	AD 3 Occipital Ctx	21.8
AD 6 Hippo	12.7	AD 4 Occipital Ctx	29.3
Control 2 Hippo	30.4	AD 5 Occipital Ctx	3.0
Control 4 Hippo	94.6	AD 6 Occipital Ctx	37.4
Control (Path) 3 Hippo	15.3	Control 1 Occipital Ctx	16.5
AD 1 Temporal Ctx	18.2	Control 2 Occipital Ctx	47.0
AD 2 Temporal Ctx	34.4	Control 3 Occipital Ctx	18.0
AD 3 Temporal Ctx	17.9	Control 4 Occipital Ctx	37.6
AD 4 Temporal Ctx	31.9	Control (Path) 1 Occipital Ctx	18.4
AD 5 Inf Temporal Ctx	100.0	Control (Path) 2 Occipital Ctx	13.9
AD 5 SupTemporal Ctx	100.0	Control (Path) 3 Occipital Ctx	12.3
AD 6 Inf Temporal Ctx	6.5	Control (Path) 4 Occipital Ctx	13.4
AD 6 Sup Temporal Ctx	11.0	Control 1 Parietal Ctx	18.2
Control 1 Temporal Ctx	19.6	Control 2 Parietal Ctx	72.7
Control 2 Temporal Ctx	40.6	Control 3 Parietal Ctx	21.3
Control 3 Temporal Ctx	20.6	Control (Path) 1 Parietal Ctx	15.2
Control 4 Temporal Ctx	61.1	Control (Path) 2 Parietal Ctx	22.2
Control (Path) 1 Temporal Ctx	14.0	Control (Path) 3 Parietal Ctx	11.6
Control (Path) 2 Temporal Ctx	31.6	Control (Path) 4 Parietal Ctx	18.2

Table ZC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3303, Run 215648467	Tissue Name	Rel. Exp.(%) Ag3303, Run 215648467
Adipose	0.1	Renal ca. TK-10	2.1
Melanoma* Hs688(A).T	20.7	Bladder	0.4
Melanoma* Hs688(B).T	15.5	Gastric ca. (liver met.) NCI-N87	100.0
Melanoma* M14	4.2	Gastric ca. KATO III	0.2
Melanoma* LOXIMVI	4.2	Colon ca. SW-948	6.2
Melanoma* SK-MEL-5	8.0	Colon ca. SW480	0.3
Squamous cell carcinoma SCC-4	0.2	Colon ca.* (SW480 met) SW620	0.1
Testis Pool	2.3	Colon ca. HT29	2.8
Prostate ca.* (bone met) PC-3	5.5	Colon ca. HCT-116	9.8
Prostate Pool	1.5	Colon ca. CaCo-2	0.4
Placenta	2.9	Colon cancer tissue	18.0
Uterus Pool	1.9	Colon ca. SW1116	0.1
Ovarian ca. OVCAR-3	0.2	Colon ca. Colo-205	5.5
Ovarian ca. SK-OV-3	23.5	Colon ca. SW-48	19.9
Ovarian ca. OVCAR-4	4.2	Colon Pool	2.0
Ovarian ca. OVCAR-5	12.1	Small Intestine Pool	3.3
Ovarian ca. IGROV-1	0.2	Stomach Pool	4.6
Ovarian ca. OVCAR-8	28.5	Bone Marrow Pool	2.8
Ovary	4.6	Fetal Heart	4.4
Breast ca. MCF-7	0.0	Heart Pool	3.5
Breast ca. MDA-MB-231	1.0	Lymph Node Pool	9.4
Breast ca. BT 549	4.1	Fetal Skeletal Muscle	0.3
Breast ca. T47D	63.7	Skeletal Muscle Pool	3.5
Breast ca. MDA-N	3.2	Spleen Pool	21.3
Breast Pool	1.9	Thymus Pool	10.9
Trachea	14.8	CNS cancer (glio/astro) U87-MG	0.1
Lung	1.5	CNS cancer (glio/astro) U-118-MG	1.2
Fetal Lung	14.0	CNS cancer (neuro;met) SK-N-AS	0.6
Lung ca. NCI-N417	0.5	CNS cancer (astro) SF-539	0.3
Lung ca. LX-1	0.0	CNS cancer (astro) SNB-75	65.5
Lung ca. NCI-H146	5.3	CNS cancer (glio) SNB-19	0.3
Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	71.2
Lung ca. A549	2.5	Brain (Amygdala) Pool	1.7
Lung ca. NCI-H526	5.8	Brain (cerebellum)	2.9
Lung ca. NCI-H23	11.7	Brain (fetal)	1.6
Lung ca. NCI-H460	0.0	Brain (Hippocampus) Pool	0.4
Lung ca. HOP-62	21.2	Cerebral Cortex Pool	0.4
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	0.8
Liver	4.0	Brain (Thalamus) Pool	1.0
Fetal Liver	1.7	Brain (whole)	1.1
Liver ca. HepG2	0.0	Spinal Cord Pool	1.4
Kidney Pool	9.6	Adrenal Gland	14.0
Fetal Kidney	2.2	Pituitary gland Pool	4.1
Renal ca. 786-0	17.8	Salivary Gland	2.8
Renal ca. A498	0.0	Thyroid (female)	3.1
Renal ca. ACHN	2.8	Pancreatic ca. CAPAN2	4.0

Renal ca. UO-31	28.7	Pancreas Pool	8.2
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Table ZD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3303, Run 164682641	Tissue Name	Rel. Exp.(%) Ag3303, Run 164682641
Secondary Th1 act	38.4	HUVEC IL-1beta	1.7
Secondary Th2 act	63.7	HUVEC IFN gamma	6.2
Secondary Tr1 act	52.1	HUVEC TNF alpha + IFN gamma	7.6
Secondary Th1 rest	1.5	HUVEC TNF alpha + IL4	3.2
Secondary Th2 rest	2.0	HUVEC IL-11	3.0
Secondary Tr1 rest	3.0	Lung Microvascular EC none	26.6
Primary Th1 act	2.7	Lung Microvascular EC TNFalpha + IL-1beta	41.5
Primary Th2 act	4.7	Microvascular Dermal EC none	18.9
Primary Tr1 act	6.0	Microvascular Dermal EC TNFalpha + IL-1beta	38.2
Primary Th1 rest	81.2	Bronchial epithelium TNFalpha + IL1beta	27.7
Primary Th2 rest	50.7	Small airway epithelium none	10.9
Primary Tr1 rest	33.0	Small airway epithelium TNFalpha + IL-1beta	24.3
CD45RA CD4 lymphocyte act	28.7	Coronary artery SMC rest	2.9
CD45RO CD4 lymphocyte act	44.4	Coronary artery SMC TNFalpha + IL-1beta	2.8
CD8 lymphocyte act	26.8	Astrocytes rest	0.9
Secondary CD8 lymphocyte rest	44.4	Astrocytes TNFalpha + IL-1beta	1.2
Secondary CD8 lymphocyte act	9.6	KU-812 (Basophil) rest	0.6
CD4 lymphocyte none	17.0	KU-812 (Basophil) PMA/ionomycin	1.7
2ry Th1/Th2/Tr1_anti-CD95 CH11	33.0	CCD1106 (Keratinocytes) none	11.7
LAK cells rest	87.7	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	28.9
LAK cells IL-2	60.3	Liver cirrhosis	3.4
LAK cells IL-2+IL-12	60.3	Lupus kidney	1.0
LAK cells IL-2+IFN gamma	77.9	NCI-H292 none	2.0
LAK cells IL-2+ IL-18	66.0	NCI-H292 IL-4	3.3
LAK cells PMA/ionomycin	100.0	NCI-H292 IL-9	3.0
NK Cells IL-2 rest	45.1	NCI-H292 IL-13	3.0
Two Way MLR 3 day	98.6	NCI-H292 IFN gamma	6.0
Two Way MLR 5 day	67.4	HPAEC none	1.8
Two Way MLR 7 day	20.0	HPAEC TNF alpha + IL-1 beta	9.5
PBMC rest	30.1	Lung fibroblast none	21.3
PBMC PWM	82.9	Lung fibroblast TNF alpha + IL-1 beta	59.0
PBMC PHA-L	52.5	Lung fibroblast IL-4	28.1
Ramos (B cell) none	29.1	Lung fibroblast IL-9	22.4
Ramos (B cell) ionomycin	45.4	Lung fibroblast IL-13	20.7
B lymphocytes PWM	24.1	Lung fibroblast IFN gamma	40.1
B lymphocytes CD40L and IL-4	12.4	Dermal fibroblast CCD1070 rest	17.8
EOL-1 dbcAMP	1.5	Dermal fibroblast CCD1070 TNF alpha	24.1
EOL-1 dbcAMP	1.1	Dermal fibroblast CCD1070 IL-1	14.5

PMA/ionomycin		beta	
Dendritic cells none	56.6	Dermal fibroblast IFN gamma	2.7
Dendritic cells LPS	29.9	Dermal fibroblast IL-4	1.4
Dendritic cells anti-CD40	41.8	IBD Colitis 2	2.7
Monocytes rest	53.6	IBD Crohn's	8.2
Monocytes LPS	66.9	Colon	5.6
Macrophages rest	88.9	Lung	46.0
Macrophages LPS	82.4	Thymus	10.7
HUVEC none	1.0	Kidney	34.9
HUVEC starved	2.5		

CNS_neurodegeneration_v1.0 Summary: Ag3303 This panel confirms the expression of this gene at moderate to high levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3303 Expression of the CG57668-01 gene is moderate to high across the majority of samples on this panel, with highest expression in a gastric cancer cell line (CT = 24.8). This gene appears to be more highly expressed in CNS, colon, gastric, renal, lung, ovarian, breast, and melanoma cancer cell lines when compared to normal tissues. The CG57668-01 gene encodes a protein that is highly homologous to HLA class I histocompatibility antigen, alpha chain H precursor (HLA-AR). The major histocompatibility complex (MHC) class I family of glycoproteins presents peptides for immunorecognition by cytotoxic T lymphocytes. Increased expression of this gene in cancer cell lines agrees with the results of other studies that found elevated levels of HLA class I antigen in tumors (ref. 1). Therefore, reduction in the expression or activity of this novel HLA class I antigen may make cancer cells sensitive to lysis by natural killer cells.

In addition, this gene is expressed at moderate levels in all regions of the central nervous system examined including amygdala, hippocampus, substantia nigra, cerebellum, cerebral cortex, thalamus and spinal cord. Class I MHC molecules, known to be important for immune responses to antigen, are expressed also by neurons that undergo activity-dependent, long-term structural and synaptic modifications (ref. 2). Specific class I MHC mRNAs are expressed by distinct mosaics of neurons, reflecting a potential for diverse neuronal functions and suggesting an important role for these molecules in the activity-dependent remodeling and plasticity of connections in the developing and mature mammalian central nervous system.

Among tissues with metabolic or endocrine function, this gene is expressed at moderate levels in adrenal gland, thyroid, pituitary gland, pancreas, skeletal muscle, heart and

liver. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes. In addition, there are significant differences of expression in fetal lung (CT = 27.8) and adult lung (CT = 30.8) as well as fetal skeletal muscle (CT = 33.2) and adult skeletal muscle (CT = 29.6). Therefore expression of this gene can be used to differentiate between fetal and adult lung as well as fetal and adult skeletal muscle.

References:

1. Sette A, Chesnut R, Fikes J. HLA expression in cancer: implications for T cell-based immunotherapy. *Immunogenetics* 2001 May-Jun;53(4):255-63.

HLA class I expression is altered in a significant fraction of the tumor types reviewed here, reflecting either immune pressure or, simply, the accumulation of pathological changes and alterations. However, in all tumor types analyzed, a majority of the tumors express HLA class I, with a general tendency for the more severe alterations to be found in later-stage and less differentiated tumors. These results are encouraging for the development of specific immunotherapies, especially considering that (1) the relatively low sensitivity of immunohistochemical techniques might underestimate HLA expression in tumors, (2) class I expression can be induced in tumor cells as a result of local inflammation and lymphokine release, and (3) class I-negative cells would be predicted to be sensitive to lysis by natural killer cells.

PMID: 11491528

2. Huh GS, Boulanger LM, Du H, Riquelme PA, Brotz TM, Shatz CJ. Functional requirement for class I MHC in CNS development and plasticity. *Science* 2000 Dec 15;290(5499):2155-9

Class I major histocompatibility complex (class I MHC) molecules, known to be important for immune responses to antigen, are expressed also by neurons that undergo activity-dependent, long-term structural and synaptic modifications. Here, we show that in mice genetically deficient for cell surface class I MHC or for a class I MHC receptor component, CD3zeta, refinement of connections between retina and central targets during development is incomplete. In the hippocampus of adult mutants, N-methyl-D aspartate receptor-dependent long-term potentiation (LTP) is enhanced, and long-term depression (LTD) is absent. Specific class I MHC messenger RNAs are expressed by distinct mosaics of neurons, reflecting a potential for diverse neuronal functions. These results demonstrate an

important role for these molecules in the activity dependent remodeling and plasticity of connections in the developing and mature mammalian central nervous system (CNS).

PMID: 11118151

Panel 4D Summary: Ag3303 The CG57668-01 gene is moderately expressed in a number of samples on this panel, with highest expression in lymphokine-activated killer (LAK) cells (CT = 26-28), independent of stimulation. This observation suggests that modulation of the expression or activity of this gene may be useful in the treatment of intracellular bacterial or viral infections. This gene is also expressed at significant levels in T cells, B cells, dendritic cells, monocytes and macrophages.

The CG57668-01 gene encodes a protein with homology to MHC class I antigen. Major histocompatibility complex (MHC) class I molecules present antigenic peptides to CD8-positive T cells. The HLA class I gene family in humans consists of 6 members: polymorphic HLA-A, HLA-B, and HLA-C, and oligomorphic HLA-E, HLA-F, and HLA-G. HLA-A/B-alleles such as the CG57664-01 gene may have utility in genotyping criminals as well as in paternity disputes. These antigens are ubiquitously expressed on all nucleated human cells except neurons and trophoblasts, and participate in antigen presentation of viral antigens in the adaptive immune response.

NOV33

Expression of NOV33/CG57672-01 was assessed using the primer-probe set Ag3305, described in Table AAA. Results of the RTQ-PCR runs are shown in Tables AAB, AAC, and AAD.

Table AAA. Probe Name Ag3305

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-aaaagtttcggtctggttctac-3'	22	1354	356
Probe	TET-5'-tttctctctgcatacgggctccagt-3'-TAMRA	26	1376	357
Reverse	5'-gaccaatggctggaagtaagt-3'	22	1412	358

Table AAB. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3305, Run 215648474	Tissue Name	Rel. Exp.(%) Ag3305, Run 215648474
Adipose	0.0	Renal ca. TK-10	1.3
Melanoma* Hs688(A).T	0.0	Bladder	0.0
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	0.0	Gastric ca. KATO III	2.4
Melanoma* LOXIMVI	0.0	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	0.0
Squamous cell carcinoma	0.0	Colon ca.* (SW480 met)	0.5

SCC-4		SW620	
Testis Pool	100.0	Colon ca. HT29	1.6
Prostate ca.* (bone met) PC-3	0.0	Colon ca. HCT-116	4.8
Prostate Pool	0.0	Colon ca. CaCo-2	1.8
Placenta	0.0	Colon cancer tissue	2.8
Uterus Pool	0.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	4.4	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	0.0	Colon Pool	1.4
Ovarian ca. OVCAR-5	0.0	Small Intestine Pool	0.8
Ovarian ca. IGROV-1	9.2	Stomach Pool	1.3
Ovarian ca. OVCAR-8	0.0	Bone Marrow Pool	2.6
Ovary	0.5	Fetal Heart	0.0
Breast ca. MCF-7	0.6	Heart Pool	2.8
Breast ca. MDA-MB-231	2.3	Lymph Node Pool	1.8
Breast ca. BT 549	0.9	Fetal Skeletal Muscle	0.0
Breast ca. T47D	1.2	Skeletal Muscle Pool	0.0
Breast ca. MDA-N	1.6	Spleen Pool	0.5
Breast Pool	2.8	Thymus Pool	1.8
Trachea	0.0	CNS cancer (glio/astro) U87-MG	0.0
Lung	0.0	CNS cancer (glio/astro) U-118-MG	1.1
Fetal Lung	0.6	CNS cancer (neuro;met) SK-N-AS	0.0
Lung ca. NCI-N417	0.5	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	1.8	CNS cancer (astro) SNB-75	2.1
Lung ca. NCI-H146	0.0	CNS cancer (glio) SNB-19	2.5
Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	2.1
Lung ca. A549	0.0	Brain (Amygdala) Pool	0.0
Lung ca. NCI-H526	0.0	Brain (cerebellum)	0.0
Lung ca. NCI-H23	3.8	Brain (fetal)	0.0
Lung ca. NCI-H460	0.0	Brain (Hippocampus) Pool	1.4
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	1.0
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	1.4
Liver	0.0	Brain (Thalamus) Pool	1.1
Fetal Liver	0.0	Brain (whole)	0.0
Liver ca. HepG2	4.6	Spinal Cord Pool	0.0
Kidney Pool	13.3	Adrenal Gland	0.0
Fetal Kidney	0.6	Pituitary gland Pool	0.0
Renal ca. 786-0	1.1	Salivary Gland	0.0
Renal ca. A498	0.0	Thyroid (female)	0.0
Renal ca. ACHN	1.0	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.0	Pancreas Pool	9.9

Table AAC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3305, Run 164682643	Tissue Name	Rel. Exp.(%) Ag3305, Run 164682643
Secondary Th1 act	11.7	HUVEC IL-1beta	4.2
Secondary Th2 act	12.2	HUVEC IFN gamma	29.9
Secondary Tr1 act	9.2	HUVEC TNF alpha + IFN gamma	6.4
Secondary Th1 rest	10.0	HUVEC TNF alpha + IL4	7.3
Secondary Th2 rest	3.3	HUVEC IL-11	7.9

Secondary Tr1 rest	27.5	Lung Microvascular EC none	19.6
Primary Th1 act	10.9	Lung Microvascular EC TNFalpha + IL-1beta	32.8
Primary Th2 act	14.6	Microvascular Dermal EC none	23.2
Primary Tr1 act	8.7	Microvascular Dermal EC TNFalpha + IL-1beta	13.3
Primary Th1 rest	20.2	Bronchial epithelium TNFalpha + IL1beta	12.0
Primary Th2 rest	11.3	Small airway epithelium none	0.0
Primary Tr1 rest	17.6	Small airway epithelium TNFalpha + IL-1beta	2.4
CD45RA CD4 lymphocyte act	5.1	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	20.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	9.5	Astrocytes rest	1.7
Secondary CD8 lymphocyte rest	19.2	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	2.4	KU-812 (Basophil) rest	24.7
CD4 lymphocyte none	5.1	KU-812 (Basophil) PMA/ionomycin	29.1
2ry Th1/Th2/Tr1_anti-CD95 CH11	18.4	CCD1106 (Keratinocytes) none	18.9
LAK cells rest	24.7	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	3.4
LAK cells IL-2	24.3	Liver cirrhosis	3.0
LAK cells IL-2+IL-12	11.2	Lupus kidney	1.8
LAK cells IL-2+IFN gamma	45.7	NCI-H292 none	18.6
LAK cells IL-2+ IL-18	13.3	NCI-H292 IL-4	34.4
LAK cells PMA/ionomycin	1.3	NCI-H292 IL-9	2.5
NK Cells IL-2 rest	3.0	NCI-H292 IL-13	1.3
Two Way MLR 3 day	27.9	NCI-H292 IFN gamma	0.8
Two Way MLR 5 day	8.0	HPAEC none	12.5
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	10.0
PBMC rest	11.7	Lung fibroblast none	5.4
PBMC PWM	19.1	Lung fibroblast TNF alpha + IL-1 beta	2.6
PBMC PHA-L	2.8	Lung fibroblast IL-4	16.2
Ramos (B cell) none	73.2	Lung fibroblast IL-9	4.1
Ramos (B cell) ionomycin	100.0	Lung fibroblast IL-13	3.5
B lymphocytes PWM	6.6	Lung fibroblast IFN gamma	15.5
B lymphocytes CD40L and IL-4	44.8	Dermal fibroblast CCD1070 rest	35.1
EOL-1 dbcAMP	4.2	Dermal fibroblast CCD1070 TNF alpha	27.4
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	1.7
Dendritic cells none	3.7	Dermal fibroblast IFN gamma	3.0
Dendritic cells LPS	14.2	Dermal fibroblast IL-4	3.3
Dendritic cells anti-CD40	11.8	IBD Colitis 2	0.5
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	8.1	Colon	1.2
Macrophages rest	21.3	Lung	0.0
Macrophages LPS	23.7	Thymus	5.9
HUVEC none	27.9	Kidney	18.6

HUVEC starved	39.2		
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Table AAD. Panel 5 Islet

Tissue Name	Rel. Exp.(%) Ag3305, Run 242322479	Tissue Name	Rel. Exp.(%) Ag3305, Run 242322479
97457_Patient-02go_adipose	0.0	94709_Donor 2 AM - A_adipose	13.0
97476_Patient-07sk_skeletal muscle	0.0	94710_Donor 2 AM - B_adipose	0.0
97477_Patient-07ut_uterus	21.6	94711_Donor 2 AM - C_adipose	100.0
97478_Patient-07pl_placenta	0.0	94712_Donor 2 AD - A_adipose	26.8
99167_Bayer Patient 1	0.0	94713_Donor 2 AD - B_adipose	0.0
97482_Patient-08ut_uterus	0.0	94714_Donor 2 AD - C_adipose	0.0
97483_Patient-08pl_placenta	23.7	94742_Donor 3 U - A_Mesenchymal Stem Cells	21.3
97486_Patient-09sk_skeletal muscle	0.0	94743_Donor 3 U - B_Mesenchymal Stem Cells	0.0
97487_Patient-09ut_uterus	3.4	94730_Donor 3 AM - A_adipose	42.0
97488_Patient-09pl_placenta	7.9	94731_Donor 3 AM - B_adipose	0.0
97492_Patient-10ut_uterus	0.0	94732_Donor 3 AM - C_adipose	17.4
97493_Patient-10pl_placenta	0.0	94733_Donor 3 AD - A_adipose	0.0
97495_Patient-11go_adipose	11.7	94734_Donor 3 AD - B_adipose	0.0
97496_Patient-11sk_skeletal muscle	8.5	94735_Donor 3 AD - C_adipose	0.0
97497_Patient-11ut_uterus	5.2	77138_Liver_HepG2untreated	84.1
97498_Patient-11pl_placenta	0.0	73556_Heart_Cardiac stromal cells (primary)	0.0
97500_Patient-12go_adipose	17.9	81735_Small Intestine	12.7
97501_Patient-12sk_skeletal muscle	15.1	72409_Kidney_Proximal Convoluted Tubule	0.0
97502_Patient-12ut_uterus	8.0	82685_Small intestine_Duodenum	0.0
97503_Patient-12pl_placenta	0.0	90650_Adrenal_Adrenocortical adenoma	0.0
94721_Donor 2 U A_Mesenchymal Stem Cells	0.0	72410_Kidney_HRCE	12.9
94722_Donor 2 U B_Mesenchymal Stem Cells	8.7	72411_Kidney_HRE	59.5
94723_Donor 2 U C_Mesenchymal Stem Cells	13.0	73139_Uterus_Uterine smooth muscle cells	0.0

CNS_neurodegeneration_v1.0 Summary: Ag3305 Results from one experiment with the CG57672-01 gene are not included because signal was high in the water-only control well (data not shown).

5 **General_screening_panel_v1.4 Summary:** Ag3305 Significant expression of the CG57672-01 gene is limited to testis (CT = 32.2). Thus, expression of this gene could be used to distinguish testis from the other samples on this panel. Furthermore, therapeutic modulation of the activity of this gene or its protein product, using small molecule drugs, antibodies or protein therapeutics, may be of use in the treatment of reproductive disorders such as

10 infertility.

Panel 4D Summary: Ag3305 The CG57672-01 gene is expressed at low levels in many of the samples on this panel, with highest expression in ionomycin-treated Ramos B

cells (CT = 31). This gene is expressed at low levels in members of the T-cell, B-cell, basophil, macrophage/dendritic cell, and peripheral blood mononuclear cell family, as well as in lung and dermal fibroblasts and microvascular endothelial cells. This ubiquitous pattern of expression suggests that this gene product may be involved in homeostatic processes for these and other cell types and tissues.

Therefore, therapeutic modulation of the activity of this gene or its protein product may lead to the alteration of functions associated with these cell types and lead to improvement of the symptoms of patients suffering from autoimmune and inflammatory diseases such as asthma, allergies, inflammatory bowel disease, lupus erythematosus, psoriasis, rheumatoid arthritis, and osteoarthritis.

Panel 5 Islet Summary: Ag3305 The CG57672-01 gene is expressed at low levels in several samples of adipocytes cultured in vitro from mesenchymal stem cells. Therefore, this gene product may be involved in adipocyte differentiation and its therapeutic modulation may be a treatment for obesity and obesity-related Type 2 diabetes.

NOV34

Expression of NOV34/CG57680-01 was assessed using the primer-probe set Ag3307, described in Table ABA. Results of the RTQ-PCR runs are shown in Tables ABB, ABC and ABD.

Table ABA. Probe Name Ag3307

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ccagaacctacaagggaacaat-3'	22	582	359
Probe	TET-5'-cacaatgaagaaattgatcattcaaacg-3'-TAMRA	30	623	360
Reverse	5'-tttacttcttcggtgacctt-3'	22	653	361

Table ABB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3307, Run 210138283	Tissue Name	Rel. Exp.(%) Ag3307, Run 210138283
AD 1 Hippo	11.6	Control (Path) 3 Temporal Ctx	23.2
AD 2 Hippo	10.4	Control (Path) 4 Temporal Ctx	36.6
AD 3 Hippo	13.8	AD 1 Occipital Ctx	44.4
AD 4 Hippo	7.9	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	100.0	AD 3 Occipital Ctx	30.8
AD 6 Hippo	18.7	AD 4 Occipital Ctx	12.5
Control 2 Hippo	9.6	AD 5 Occipital Ctx	34.6
Control 4 Hippo	11.6	AD 6 Occipital Ctx	13.7
Control (Path) 3 Hippo	15.7	Control 1 Occipital Ctx	10.0
AD 1 Temporal Ctx	22.4	Control 2 Occipital Ctx	14.0
AD 2 Temporal Ctx	23.8	Control 3 Occipital Ctx	40.6
AD 3 Temporal Ctx	19.5	Control 4 Occipital Ctx	13.0

AD 4 Temporal Ctx	19.5	Control (Path) 1 Occipital Ctx	36.1
AD 5 Inf Temporal Ctx	85.3	Control (Path) 2 Occipital Ctx	36.3
AD 5 Sup Temporal Ctx	34.6	Control (Path) 3 Occipital Ctx	11.7
AD 6 Inf Temporal Ctx	36.1	Control (Path) 4 Occipital Ctx	52.9
AD 6 Sup Temporal Ctx	44.1	Control 1 Parietal Ctx	17.2
Control 1 Temporal Ctx	16.5	Control 2 Parietal Ctx	63.7
Control 2 Temporal Ctx	13.1	Control 3 Parietal Ctx	22.4
Control 3 Temporal Ctx	18.3	Control (Path) 1 Parietal Ctx	32.5
Control 4 Temporal Ctx	22.1	Control (Path) 2 Parietal Ctx	28.5
Control (Path) 1 Temporal Ctx	29.7	Control (Path) 3 Parietal Ctx	24.5
Control (Path) 2 Temporal Ctx	25.9	Control (Path) 4 Parietal Ctx	49.7

Table ABC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3307, Run 215648237	Tissue Name	Rel. Exp.(%) Ag3307, Run 215648237
Adipose	1.1	Renal ca. TK-10	1.8
Melanoma* Hs688(A).T	0.2	Bladder	4.0
Melanoma* Hs688(B).T	0.5	Gastric ca. (liver met.) NCI-N87	1.4
Melanoma* M14	0.6	Gastric ca. KATO III	1.6
Melanoma* LOXIMV1	0.6	Colon ca. SW-948	0.5
Melanoma* SK-MEL-5	1.4	Colon ca. SW480	1.9
Squamous cell carcinoma SCC-4	0.9	Colon ca.* (SW480 met) SW620	1.3
Testis Pool	1.8	Colon ca. HT29	1.3
Prostate ca.* (bone met) PC-3	1.2	Colon ca. HCT-116	1.3
Prostate Pool	2.2	Colon ca. CaCo-2	2.7
Placenta	3.3	Colon cancer tissue	1.8
Uterus Pool	0.4	Colon ca. SW1116	1.8
Ovarian ca. OVCAR-3	1.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	0.9	Colon ca. SW-48	0.4
Ovarian ca. OVCAR-4	0.1	Colon Pool	100.0
Ovarian ca. OVCAR-5	4.2	Small Intestine Pool	3.0
Ovarian ca. IGROV-1	5.2	Stomach Pool	4.3
Ovarian ca. OVCAR-8	1.1	Bone Marrow Pool	1.8
Ovary	1.2	Fetal Heart	3.5
Breast ca. MCF-7	3.4	Heart Pool	1.1
Breast ca. MDA-MB-231	3.2	Lymph Node Pool	2.9
Breast ca. BT 549	3.6	Fetal Skeletal Muscle	2.6
Breast ca. T47D	7.8	Skeletal Muscle Pool	1.3
Breast ca. MDA-N	0.9	Spleen Pool	13.8
Breast Pool	4.2	Thymus Pool	16.7
Trachea	3.9	CNS cancer (glio/astro) U87-MG	2.0
Lung	3.5	CNS cancer (glio/astro) U-118-MG	6.4
Fetal Lung	40.9	CNS cancer (neuro;met) SK-N-AS	3.7

Lung ca. NCI-N417	3.2	CNS cancer (astro) SF-539	0.3
Lung ca. LX-1	1.1	CNS cancer (astro) SNB-75	2.5
Lung ca. NCI-H146	1.5	CNS cancer (glio) SNB-19	4.0
Lung ca. SHP-77	4.8	CNS cancer (glio) SF-295	3.2
Lung ca. A549	0.0	Brain (Amygdala) Pool	1.8
Lung ca. NCI-H526	0.6	Brain (cerebellum)	2.8
Lung ca. NCI-H23	1.1	Brain (fetal)	5.2
Lung ca. NCI-H460	5.3	Brain (Hippocampus) Pool	2.1
Lung ca. HOP-62	1.6	Cerebral Cortex Pool	2.7
Lung ca. NCI-H522	1.2	Brain (Substantia nigra) Pool	2.3
Liver	0.0	Brain (Thalamus) Pool	4.2
Fetal Liver	1.1	Brain (whole)	1.1
Liver ca. HepG2	0.1	Spinal Cord Pool	1.7
Kidney Pool	4.4	Adrenal Gland	0.7
Fetal Kidney	9.8	Pituitary gland Pool	0.8
Renal ca. 786-0	3.0	Salivary Gland	0.5
Renal ca. A498	1.2	Thyroid (female)	1.8
Renal ca. ACHN	0.8	Pancreatic ca. CAPAN2	2.6
Renal ca. UO-31	0.3	Pancreas Pool	3.4

Table ABD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3307, Run 164335286	Tissue Name	Rel. Exp.(%) Ag3307, Run 164335286
Secondary Th1 act	3.1	HUVEC IL-1beta	0.8
Secondary Th2 act	4.7	HUVEC IFN gamma	3.5
Secondary Tr1 act	6.1	HUVEC TNF alpha + IFN gamma	2.2
Secondary Th1 rest	6.7	HUVEC TNF alpha + IL4	0.6
Secondary Th2 rest	5.0	HUVEC IL-11	0.8
Secondary Tr1 rest	7.4	Lung Microvascular EC none	0.4
Primary Th1 act	4.6	Lung Microvascular EC TNFalpha + IL-1beta	0.2
Primary Th2 act	6.0	Microvascular Dermal EC none	0.7
Primary Tr1 act	9.9	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	37.6	Bronchial epithelium TNFalpha + IL1beta	1.3
Primary Th2 rest	24.5	Small airway epithelium none	0.7
Primary Tr1 rest	13.5	Small airway epithelium TNFalpha + IL-1beta	3.3
CD45RA CD4 lymphocyte act	2.5	Coronary artery SMC rest	0.3
CD45RO CD4 lymphocyte act	8.6	Coronary artery SMC TNFalpha + IL-1beta	0.4
CD8 lymphocyte act	4.6	Astrocytes rest	1.1
Secondary CD8 lymphocyte rest	3.3	Astrocytes TNFalpha + IL-1beta	1.8
Secondary CD8 lymphocyte act	8.0	KU-812 (Basophil) rest	3.8
CD4 lymphocyte none	6.3	KU-812 (Basophil) PMA/ionomycin	8.7
2ry Th1/Th2/Tr1_anti-CD95 CH11	14.9	CCD1106 (Keratinocytes) none	1.2
LAK cells rest	5.6	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	20.4	Liver cirrhosis	1.8
LAK cells IL-2+IL-12	6.0	Lupus kidney	1.5

LAK cells IL-2+IFN gamma	9.8	NCI-H292 none	15.2
LAK cells IL-2+ IL-18	10.3	NCI-H292 IL-4	7.8
LAK cells PMA/ionomycin	1.7	NCI-H292 IL-9	18.2
NK Cells IL-2 rest	14.2	NCI-H292 IL-13	7.0
Two Way MLR 3 day	14.9	NCI-H292 IFN gamma	8.5
Two Way MLR 5 day	3.0	HPAEC none	1.7
Two Way MLR 7 day	8.1	HPAEC TNF alpha + IL-1 beta	0.3
PBMC rest	5.1	Lung fibroblast none	2.6
PBMC PWM	13.8	Lung fibroblast TNF alpha + IL-1 beta	2.2
PBMC PHA-L	6.7	Lung fibroblast IL-4	4.0
Ramos (B cell) none	10.7	Lung fibroblast IL-9	2.8
Ramos (B cell) ionomycin	24.0	Lung fibroblast IL-13	2.5
B lymphocytes PWM	24.1	Lung fibroblast IFN gamma	3.7
B lymphocytes CD40L and IL-4	54.3	Dermal fibroblast CCD1070 rest	3.5
EOL-1 dbcAMP	1.7	Dermal fibroblast CCD1070 TNF alpha	18.8
EOL-1 dbcAMP PMA/ionomycin	1.8	Dermal fibroblast CCD1070 IL-1 beta	0.8
Dendritic cells none	1.4	Dermal fibroblast IFN gamma	1.4
Dendritic cells LPS	0.4	Dermal fibroblast IL-4	1.0
Dendritic cells anti-CD40	0.5	IBD Colitis 2	3.3
Monocytes rest	1.1	IBD Crohn's	2.2
Monocytes LPS	0.7	Colon	7.2
Macrophages rest	2.8	Lung	1.6
Macrophages LPS	0.3	Thymus	8.8
HUVEC none	1.7	Kidney	100.0
HUVEC starved	4.5		

CNS_neurodegeneration_v1.0 Summary: Ag3307 This panel confirms the expression of this gene at low to moderate levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3307 The CG57680-01 gene is expressed at low levels in many of the tissues on this panel, with the highest expression in a normal colon sample (CT = 28.8). Significant expression of this gene is also detected in fetal lung (CT = 30.1). Interestingly, this gene is expressed at much lower levels in adult lung (CT = 33.6), suggesting that expression of this gene can be used to distinguish fetal lung from adult lung.

This gene is also expressed at low levels in many regions of the central nervous system, including amygdala, substantia nigra, thalamus, hippocampus, cerebellum, cerebral cortex, and spinal cord. The CG57680-01 gene encodes a protein with homology to

cyclophilin-type peptidyl-prolyl cis-trans isomerase. Cyclophilin is a specific high-affinity binding protein for the immunosuppressant agent cyclosporin A. Neuroimmunophilin ligands, such as cyclosporin A, are a class of compounds that hold great promise for the treatment of nerve injuries and neurological disease. Therefore, modulation of the activity of the CG57680-01 gene or its protein product may be of use in the treatment of neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease.

Among tissues with metabolic or endocrine function, this gene is expressed at low levels in thyroid, pancreas, fetal heart, and fetal skeletal muscle. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

References:

1. Gold BG. Neuroimmunophilin ligands: evaluation of their therapeutic potential for the treatment of neurological disorders. *Expert Opin Investig Drugs* 2000 Oct;9(10):2331-42

Neuroimmunophilin ligands are a class of compounds that hold great promise for the treatment of nerve injuries and neurological disease. In contrast to neurotrophins (e.g., nerve growth factor), these compounds readily cross the blood-brain barrier, being orally effective in a variety of animal models of ischaemia, traumatic nerve injury and human neurodegenerative disorders. A further distinction is that neuroimmunophilin ligands act via unique receptors that are unrelated to the classical neurotrophic receptors e.g., trk), making it unlikely that clinical trials will encounter the same difficulties found with the neurotrophins. Another advantage is that two neuroimmunophilin ligands (cyclosporin A and FK-506) have already been used in humans (as immunosuppressant drugs). Whereas both cyclosporin A and FK-506 demonstrate neuroprotective actions, only FK-506 and its derivatives have been clearly shown to exhibit significant neuroregenerative activity. Accordingly, the neuroprotective and neuroregenerative properties seem to arise via different mechanisms. Furthermore, the neuroregenerative property does not involve calcineurin inhibition (essential for immunosuppression). This is important since most of the limiting side effects produced by these drugs arise via calcineurin inhibition. A major breakthrough for the development of this class of compounds for the treatment of human neurological disorders was the ability to separate the neuroregenerative property of FK-506 from its immunosuppressant action via the development of non-immunosuppressant (non-calcineurin inhibiting) derivatives. Further studies revealed that different receptor subtypes, or FK-506-binding proteins (FKBPs), mediate immunosuppression and nerve regeneration (FKBP-12 and FKBP-52, respectively, the latter

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PMID: 11060810

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NOV35

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Table ACA. Probe Name Ag3304

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-aaagcttgctctgactccat-3'	22	297	362
Probe	TET-5'-cctaccagcccatgctgtgacct-3'-TAMRA	24	320	363
Reverse	5'-ttgggatctcagggtcctttagt-3'	22	350	364

Table ACB. CNS neurodegeneration v1.0

Tissue Name	Rel. Exp.(%) Ag3304, Run 210063833	Tissue Name	Rel. Exp.(%) Ag3304, Run 210063833
AD 1 Hippo	2.0	Control (Path) 3 Temporal Ctx	1.2
AD 2 Hippo	22.2	Control (Path) 4 Temporal Ctx	14.9
AD 3 Hippo	3.2	AD 1 Occipital Ctx	17.3
AD 4 Hippo	24.1	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	45.4	AD 3 Occipital Ctx	7.5
AD 6 Hippo	70.2	AD 4 Occipital Ctx	48.3
Control 2 Hippo	51.8	AD 5 Occipital Ctx	9.0
Control 4 Hippo	18.2	AD 6 Occipital Ctx	15.7
Control (Path) 3 Hippo	14.8	Control 1 Occipital Ctx	3.1
AD 1 Temporal Ctx	8.0	Control 2 Occipital Ctx	50.0
AD 2 Temporal Ctx	85.3	Control 3 Occipital Ctx	24.0
AD 3 Temporal Ctx	4.1	Control 4 Occipital Ctx	11.7

AD 4 Temporal Ctx	23.3	Control (Path) 1 Occipital Ctx	57.0
AD 5 Inf Temporal Ctx	11.3	Control (Path) 2 Occipital Ctx	21.5
AD 5 Sup Temporal Ctx	49.7	Control (Path) 3 Occipital Ctx	5.5
AD 6 Inf Temporal Ctx	31.6	Control (Path) 4 Occipital Ctx	12.2
AD 6 Sup Temporal Ctx	29.3	Control 1 Parietal Ctx	17.2
Control 1 Temporal Ctx	16.6	Control 2 Parietal Ctx	13.8
Control 2 Temporal Ctx	46.0	Control 3 Parietal Ctx	16.3
Control 3 Temporal Ctx	41.8	Control (Path) 1 Parietal Ctx	70.2
Control 3 Temporal Ctx	3.6	Control (Path) 2 Parietal Ctx	21.3
Control (Path) 1 Temporal Ctx	100.0	Control (Path) 3 Parietal Ctx	5.4
Control (Path) 2 Temporal Ctx	89.5	Control (Path) 4 Parietal Ctx	15.0

Table ACC. General screening panel v1.4

Tissue Name	Rel. Exp.(%) Ag3304, Run 215648468	Tissue Name	Rel. Exp.(%) Ag3304, Run 215648468
Adipose	0.0	Renal ca. TK-10	0.0
Melanoma* Hs688(A).T	0.0	Bladder	0.0
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	0.0	Colon ca. SW-948	100.0
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	0.0
Squamous cell carcinoma SCC-4	0.0	Colon ca.* (SW480 met) SW620	0.0
Testis Pool	0.0	Colon ca. HT29	0.0
Prostate ca.* (bone met) PC-3	0.0	Colon ca. HCT-116	0.0
Prostate Pool	0.0	Colon ca. CaCo-2	0.0
Placenta	0.0	Colon cancer tissue	0.0
Uterus Pool	0.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	0.0	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	0.0	Colon Pool	0.0
Ovarian ca. OVCAR-5	0.0	Small Intestine Pool	0.0
Ovarian ca. IGROV-1	0.0	Stomach Pool	0.0
Ovarian ca. OVCAR-8	0.0	Bone Marrow Pool	0.0
Ovary	0.0	Fetal Heart	0.0
Breast ca. MCF-7	0.0	Heart Pool	0.0
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	0.0
Breast ca. BT 549	0.0	Fetal Skeletal Muscle	0.0
Breast ca. T47D	0.0	Skeletal Muscle Pool	0.0
Breast ca. MDA-N	0.0	Spleen Pool	0.0
Breast Pool	0.0	Thymus Pool	0.0
Trachea	0.0	CNS cancer (glio/astro) U87-MG	0.0
Lung	0.0	CNS cancer (glio/astro) U-118-MG	0.0
Fetal Lung	0.0	CNS cancer (neuro;met) SK-N-AS	0.0

Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	0.0	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	0.0	CNS cancer (glio) SNB-19	0.0
Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	0.0
Lung ca. A549	0.0	Brain (Amygdala) Pool	0.0
Lung ca. NCI-H526	0.0	Brain (cerebellum)	0.0
Lung ca. NCI-H23	0.0	Brain (fetal)	0.0
Lung ca. NCI-H460	0.0	Brain (Hippocampus) Pool	0.0
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	0.0
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	0.0
Liver	0.0	Brain (Thalamus) Pool	0.0
Fetal Liver	0.0	Brain (whole)	0.0
Liver ca. HepG2	0.0	Spinal Cord Pool	0.0
Kidney Pool	0.0	Adrenal Gland	0.0
Fetal Kidney	0.0	Pituitary gland Pool	0.0
Renal ca. 786-0	0.0	Salivary Gland	0.0
Renal ca. A498	0.0	Thyroid (female)	0.0
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.0	Pancreas Pool	0.0

Table ACD. General_screening_panel_v1.5

Tissue Name	Rel. Exp.(%) Ag3304, Run 244373099	Rel. Exp.(%) Ag3304, Run 248445829	Tissue Name	Rel. Exp.(%) Ag3304, Run 244373099	Rel. Exp.(%) Ag3304, Run 248445829
Adipose	0.5	5.6	Renal ca. TK-10	8.1	6.2
Melanoma* Hs688(A).T	15.0	0.0	Bladder	4.6	35.6
Melanoma* Hs688(B).T	19.9	1.0	Gastric ca. (liver met.) NCI-N87	3.2	11.4
Melanoma* M14	17.3	0.5	Gastric ca. KATO III	3.4	18.4
Melanoma* LOXIMVI	13.7	0.7	Colon ca. SW-948	0.6	39.8
Melanoma* SK- MEL-5	11.0	0.0	Colon ca. SW480	7.6	6.2
Squamous cell carcinoma SCC-4	15.6	47.3	Colon ca.* (SW480 met) SW620	4.1	5.3
Testis Pool	1.1	4.9	Colon ca. HT29	6.3	3.8
Prostate ca.* (bone met) PC-3	11.6	19.3	Colon ca. HCT-116	2.6	5.8
Prostate Pool	3.8	1.7	Colon ca. CaCo-2	0.7	4.7
Placenta	0.0	5.1	Colon cancer tissue	0.0	11.2
Uterus Pool	0.3	1.9	Colon ca. SW1116	7.8	2.1
Ovarian ca. OVCA-3	0.0	2.1	Colon ca. Colo-205	4.0	39.8
Ovarian ca. SK- OV-3	1.1	13.7	Colon ca. SW-48	4.4	4.3
Ovarian ca. OVCA-4	5.0	100.0	Colon Pool	0.0	1.3
Ovarian ca. OVCA-5	6.4	43.2	Small Intestine Pool	0.7	4.4
Ovarian ca. IGROV-1	1.1	26.6	Stomach Pool	1.0	22.4
Ovarian ca. OVCA-8	11.3	5.8	Bone Marrow Pool	3.7	5.4
Ovary	0.3	13.7	Fetal Heart	0.0	12.0
Breast ca. MCF-7	3.8	3.6	Heart Pool	0.3	12.4

Breast ca. MDA-MB-231	1.3	3.3	Lymph Node Pool	0.2	5.6
Breast ca. BT 549	3.6	0.9	Fetal Skeletal Muscle	0.8	1.4
Breast ca. T47D	0.3	0.9	Skeletal Muscle Pool	0.9	3.1
Breast ca. MDA-N	0.2	3.0	Spleen Pool	2.2	12.2
Breast Pool	0.0	6.6	Thymus Pool	2.1	7.3
Trachea	0.0	5.4	CNS cancer (glio/astro) U87-MG	0.8	1.3
Lung	0.0	7.9	CNS cancer (glio/astro) U-118-MG	2.7	22.7
Fetal Lung	0.4	13.9	CNS cancer (neuro;met) SK-N-AS	3.4	1.2
Lung ca. NCI-N417	2.1	0.9	CNS cancer (astro) SF-539	2.8	4.3
Lung ca. LX-1	24.3	9.7	CNS cancer (astro) SNB-75	5.0	15.4
Lung ca. NCI-H146	0.7	0.0	CNS cancer (glio) SNB-19	1.4	28.5
Lung ca. SHP-77	5.1	12.1	CNS cancer (glio) SF-295	16.2	45.1
Lung ca. A549	19.9	3.9	Brain (Amygdala) Pool	4.3	8.4
Lung ca. NCI-H526	2.1	0.7	Brain (cerebellum)	3.2	3.1
Lung ca. NCI-H23	29.5	63.7	Brain (fetal)	1.3	5.6
Lung ca. NCI-H460	100.0	18.4	Brain (Hippocampus) Pool	0.5	2.8
Lung ca. HOP-62	16.7	4.1	Cerebral Cortex Pool	0.9	3.1
Lung ca. NCI-H522	3.0	1.6	Brain (Substantia nigra) Pool	4.1	31.0
Liver	0.4	2.3	Brain (Thalamus) Pool	3.3	5.4
Fetal Liver	0.0	5.0	Brain (whole)	0.0	17.0
Liver ca. HepG2	3.3	4.8	Spinal Cord Pool	0.3	2.7
Kidney Pool	1.4	4.0	Adrenal Gland	15.7	4.6
Fetal Kidney	1.2	4.2	Pituitary gland Pool	0.0	36.9
Renal ca. 786-0	20.0	9.2	Salivary Gland	0.0	0.0
Renal ca. A498	3.4	16.5	Thyroid (female)	0.3	8.2
Renal ca. ACHN	6.3	8.7	Pancreatic ca. CAPAN2	11.1	26.2
Renal ca. UO-31	7.6	6.3	Pancreas Pool	1.9	19.9

Table ACE. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3304, Run 164682642	Tissue Name	Rel. Exp.(%) Ag3304, Run 164682642
Secondary Th1 act	9.4	HUVEC IL-1beta	8.6
Secondary Th2 act	9.3	HUVEC IFN gamma	11.7
Secondary Tr1 act	20.9	HUVEC TNF alpha + IFN gamma	27.0
Secondary Th1 rest	3.5	HUVEC TNF alpha + IL4	14.4
Secondary Th2 rest	2.1	HUVEC IL-11	15.0
Secondary Tr1 rest	1.5	Lung Microvascular EC none	8.0
Primary Th1 act	10.1	Lung Microvascular EC TNFalpha + IL-1beta	13.3
Primary Th2 act	8.7	Microvascular Dermal EC none	6.1
Primary Tr1 act	25.0	Microvascular Dermal EC	15.2

		TNFalpha + IL-1beta	
Primary Th1 rest	25.9	Bronchial epithelium TNFalpha + IL1beta	54.3
Primary Th2 rest	8.9	Small airway epithelium none	20.4
Primary Tr1 rest	5.4	Small airway epithelium TNFalpha + IL-1beta	51.4
CD45RA CD4 lymphocyte act	5.4	Coronary artery SMC rest	30.1
CD45RO CD4 lymphocyte act	25.2	Coronary artery SMC TNFalpha + IL-1beta	10.2
CD8 lymphocyte act	43.2	Astrocytes rest	17.7
Secondary CD8 lymphocyte rest	31.0	Astrocytes TNFalpha + IL-1beta	25.7
Secondary CD8 lymphocyte act	13.6	KU-812 (Basophil) rest	4.0
CD4 lymphocyte none	1.6	KU-812 (Basophil) PMA/ionomycin	20.3
2ry Th1/Th2/Tr1_anti-CD95 CH11	6.2	CCD1106 (Keratinocytes) none	21.0
LAK cells rest	5.3	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	58.6
LAK cells IL-2	11.9	Liver cirrhosis	2.7
LAK cells IL-2+IL-12	11.5	Lupus kidney	3.7
LAK cells IL-2+IFN gamma	11.2	NCI-H292 none	31.2
LAK cells IL-2+ IL-18	17.9	NCI-H292 IL-4	58.2
LAK cells PMA/ionomycin	18.3	NCI-H292 IL-9	100.0
NK Cells IL-2 rest	17.1	NCI-H292 IL-13	1.4
Two Way MLR 3 day	12.1	NCI-H292 IFN gamma	35.6
Two Way MLR 5 day	6.4	HPAEC none	12.5
Two Way MLR 7 day	10.7	HPAEC TNF alpha + IL-1 beta	21.0
PBMC rest	3.3	Lung fibroblast none	21.0
PBMC PWM	33.9	Lung fibroblast TNF alpha + IL-1 beta	11.6
PBMC PHA-L	33.9	Lung fibroblast IL-4	18.8
Ramos (B cell) none	8.0	Lung fibroblast IL-9	26.4
Ramos (B cell) ionomycin	32.5	Lung fibroblast IL-13	20.9
B lymphocytes PWM	36.9	Lung fibroblast IFN gamma	67.4
B lymphocytes CD40L and IL-4	11.3	Dermal fibroblast CCD1070 rest	62.0
EOL-1 dbcAMP	1.9	Dermal fibroblast CCD1070 TNF alpha	94.6
EOL-1 dbcAMP PMA/ionomycin	23.0	Dermal fibroblast CCD1070 IL-1 beta	16.7
Dendritic cells none	15.4	Dermal fibroblast IFN gamma	16.4
Dendritic cells LPS	34.9	Dermal fibroblast IL-4	43.5
Dendritic cells anti-CD40	9.5	IBD Colitis 2	0.3
Monocytes rest	16.4	IBD Crohn's	0.8
Monocytes LPS	12.9	Colon	12.1
Macrophages rest	30.8	Lung	9.0
Macrophages LPS	29.5	Thymus	0.7
HUVEC none	13.5	Kidney	10.2
HUVEC starved	38.4		

Table ACE. Panel 5 Islet

Tissue Name	Rel. Exp.(%) Ag3304, Run 242322478	Tissue Name	Rel. Exp.(%) Ag3304, Run 242322478
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97457_Patient-02go_adipose	9.0	94709_Donor 2 AM - A_adipose	12.1
97476_Patient-07sk_skeletal muscle	11.2	94710_Donor 2 AM - B_adipose	6.1
97477_Patient-07ut_uterus	20.0	94711_Donor 2 AM - C_adipose	2.4
97478_Patient-07pl_placenta	8.1	94712_Donor 2 AD - A_adipose	19.6
99167_Bayer Patient 1	42.3	94713_Donor 2 AD - B_adipose	16.8
97482_Patient-08ut_uterus	8.8	94714_Donor 2 AD - C_adipose	15.8
97483_Patient-08pl_placenta	4.6	94742_Donor 3 U - A_Mesenchymal Stem Cells	4.9
97486_Patient-09sk_skeletal muscle	6.2	94743_Donor 3 U - B_Mesenchymal Stem Cells	6.4
97487_Patient-09ut_uterus	12.4	94730_Donor 3 AM - A_adipose	10.8
97488_Patient-09pl_placenta	3.9	94731_Donor 3 AM - B_adipose	8.0
97492_Patient-10ut_uterus	8.0	94732_Donor 3 AM - C_adipose	6.2
97493_Patient-10pl_placenta	3.4	94733_Donor 3 AD - A_adipose	32.8
97495_Patient-11go_adipose	2.0	94734_Donor 3 AD - B_adipose	11.7
97496_Patient-11sk_skeletal muscle	4.7	94735_Donor 3 AD - C_adipose	23.5
97497_Patient-11ut_uterus	2.9	77138_Liver_HepG2untreated	9.2
97498_Patient-11pl_placenta	1.8	73556_Heart_Cardiac stromal cells (primary)	2.4
97500_Patient-12go_adipose	4.2	81735_Small Intestine	3.8
97501_Patient-12sk_skeletal muscle	14.1	72409_Kidney_Proximal Convoluted Tubule	16.8
97502_Patient-12ut_uterus	3.5	82685_Small intestine_Duodenum	4.1
97503_Patient-12pl_placenta	0.9	90650_Adrenal_Adrenocortical adenoma	2.4
94721_Donor 2 U - A_Mesenchymal Stem Cells	8.9	72410_Kidney_HRCE	100.0
94722_Donor 2 U - B_Mesenchymal Stem Cells	4.3	72411_Kidney_HRE	36.1
94723_Donor 2 U - C_Mesenchymal Stem Cells	9.1	73139_Uterus_Uterine smooth muscle cells	20.6

CNS_neurodegeneration_v1.0 Summary: Ag3304 This panel demonstrates the expression of this gene at low levels in the brain in several different individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment.

5 **General_screening_panel_v1.4 Summary:** Ag3304 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

10 **General_screening_panel_v1.5 Summary:** Ag3304 Results from two experiments using the same probe/primer set gave results that are only in moderate agreement. Only those results that are in agreement will be discussed here. Expression of the CG57670-01 gene is detected at low levels in pancreatic cancer cell line CAPAN2, CNS cancer cell line SF-295, lung cancer cell lines NCI-H460 and NCI-H23, and squamous cell carcinoma cell line SCC-4. Thus, expression of this gene can be used to distinguish these cell lines from the other samples on this panel. In addition, therapeutic modulation of the activity of this gene or its protein product, through the use of small molecule drugs, protein therapeutics or antibodies, might be

beneficial in the treatment of lung cancer, pancreatic cancer, CNS cancer and squamous cell carcinoma.

In one experiment, this gene is expressed at low levels in the adrenal gland. As a glycolytic enzyme, activation of the CG57670-01 gene may increase oxidative metabolism in this tissue and be a treatment for Addison's disease and other adrenalopathies.

Panel 4D Summary: Ag3304 The CG57670-01 gene is expressed at low to moderate levels in a wide range of cell types of significance in the immune response in health and disease. These cells include members of the T-cell, B-cell, endothelial cell, macrophage/monocyte, and peripheral blood mononuclear cell family, as well as epithelial and fibroblast cell types from lung and skin, and normal tissues represented by colon, lung, and kidney. This ubiquitous pattern of expression suggests that this gene product may be involved in homeostatic processes for these and other cell types and tissues.

Therefore, modulation of the gene product with a functional therapeutic may lead to the alteration of functions associated with these cell types and lead to improvement of the symptoms of patients suffering from autoimmune and inflammatory diseases such as asthma, allergies, inflammatory bowel disease, lupus erythematosus, psoriasis, rheumatoid arthritis, and osteoarthritis.

Panel 5 Islet Summary: Ag3304 The CG57670-01 gene is expressed at moderate levels in islets of Langerhans (patient 1). Insulin secretion is dependent on glycolysis, and activation of this glycolytic enzyme may increase the glycolytic rate and insulin secretion in Type 2 diabetes. This gene is also expressed at low levels in adipose, cultured adipocytes, skeletal muscle, uterus and placenta. Therefore, activation of this enzyme may also be a treatment for obesity by increasing the glycolytic rate and energy expenditure in adipose tissue.

NOV36

Expression of NOV36A/CG57149-01 and NOV36B/CG57149-02 was assessed using the primer-probe set Ag3119, described in Table DA. Results of the RTQ-PCR runs are shown in Tables DB, DC, DD and DE. Please note that CG57149-02 represents a full-length physical clone of the CG57149-01 gene, validating the prediction of the gene sequence.

Table DA. Probe Name Ag3119

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-tgtactaccagccatggtcaac-3'	22	12	365

Probe	TET-5'-catgttcttcaacatgccatcaaca-3'-TAMRA	26	39	366
Reverse	5'-acttgctgcaaacagttcgaa-3'	22	88	367

Table DB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3119, Run 208976882	Tissue Name	Rel. Exp.(%) Ag3119, Run 208976882
AD 1 Hippo	3.8	Control (Path) 3 Temporal Ctx	8.4
AD 2 Hippo	7.0	Control (Path) 4 Temporal Ctx	35.8
AD 3 Hippo	14.5	AD 1 Occipital Ctx	36.3
AD 4 Hippo	1.5	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	100.0	AD 3 Occipital Ctx	18.4
AD 6 Hippo	4.8	AD 4 Occipital Ctx	7.1
Control 2 Hippo	1.7	AD 5 Occipital Ctx	0.7
Control 4 Hippo	1.2	AD 6 Occipital Ctx	36.3
Control (Path) 3 Hippo	2.2	Control 1 Occipital Ctx	0.6
AD 1 Temporal Ctx	16.4	Control 2 Occipital Ctx	3.7
AD 2 Temporal Ctx	12.2	Control 3 Occipital Ctx	49.0
AD 3 Temporal Ctx	16.6	Control 4 Occipital Ctx	3.0
AD 4 Temporal Ctx	19.8	Control (Path) 1 Occipital Ctx	29.9
AD 5 Inf Temporal Ctx	35.8	Control (Path) 2 Occipital Ctx	15.8
AD 5 Sup Temporal Ctx	41.2	Control (Path) 3 Occipital Ctx	7.4
AD 6 Inf Temporal Ctx	16.4	Control (Path) 4 Occipital Ctx	42.9
AD 6 Sup Temporal Ctx	35.6	Control 1 Parietal Ctx	10.4
Control 1 Temporal Ctx	7.9	Control 2 Parietal Ctx	40.9
Control 2 Temporal Ctx	0.0	Control 3 Parietal Ctx	5.2
Control 3 Temporal Ctx	4.7	Control (Path) 1 Parietal Ctx	5.2
Control 3 Temporal Ctx	4.0	Control (Path) 2 Parietal Ctx	8.9
Control (Path) 1 Temporal Ctx	14.9	Control (Path) 3 Parietal Ctx	5.7
Control (Path) 2 Temporal Ctx	20.0	Control (Path) 4 Parietal Ctx	44.1

Table DC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag3119, Run 167985261	Tissue Name	Rel. Exp.(%) Ag3119, Run 167985261
Liver adenocarcinoma	1.2	Kidney (fetal)	16.3
Pancreas	0.6	Renal ca. 786-0	7.1
Pancreatic ca. CAPAN 2	27.9	Renal ca. A498	0.0
Adrenal gland	0.9	Renal ca. RXF 393	7.9
Thyroid	0.0	Renal ca. ACHN	26.6
Salivary gland	3.3	Renal ca. UO-31	0.0
Pituitary gland	1.0	Renal ca. TK-10	34.9
Brain (fetal)	100.0	Liver	5.5
Brain (whole)	3.2	Liver (fetal)	0.5
Brain (amygdala)	12.7	Liver ca. (hepatoblast) HepG2	44.4
Brain (cerebellum)	68.3	Lung	6.7
Brain (hippocampus)	1.0	Lung (fetal)	0.0

Brain (substantia nigra)	5.1	Lung ca. (small cell) LX-1	1.0
Brain (thalamus)	9.9	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	6.7	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	18.2	Lung ca. (large cell) NCI-H460	0.0
glio/astro U87-MG	1.1	Lung ca. (non-sm. cell) A549	7.1
glio/astro U-118-MG	1.5	Lung ca. (non-s.cell) NCI-H23	0.5
astrocytoma SW1783	2.1	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	1.4	Lung ca. (non-s.cl) NCI-H522	2.0
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	1.5	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	1.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	6.5	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	8.1	Breast ca. BT-549	5.6
Skeletal muscle (fetal)	9.9	Breast ca. MDA-N	0.0
Skeletal muscle	4.1	Ovary	0.0
Bone marrow	3.1	Ovarian ca. OVCAR-3	0.0
Thymus	97.3	Ovarian ca. OVCAR-4	0.0
Spleen	9.5	Ovarian ca. OVCAR-5	0.0
Lymph node	19.8	Ovarian ca. OVCAR-8	0.7
Colorectal	24.5	Ovarian ca. IGROV-1	0.0
Stomach	18.8	Ovarian ca.* (ascites) SK-OV-3	11.5
Small intestine	22.7	Uterus	10.8
Colon ca. SW480	0.0	Placenta	0.0
Colon ca.* SW620(SW480 met)	4.3	Prostate	5.6
Colon ca. HT29	0.0	Prostate ca.* (bone met) PC-3	0.0
Colon ca. HCT-116	2.1	Testis	4.3
Colon ca. CaCo-2	16.4	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.5
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	1.7	Melanoma LOX IMVI	0.0
Trachea	1.6	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table DD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3119, Run 164526109	Tissue Name	Rel. Exp.(%) Ag3119, Run 164526109
Secondary Th1 act	5.7	HUVEC IL-1beta	3.3
Secondary Th2 act	8.8	HUVEC IFN gamma	19.5
Secondary Tr1 act	11.3	HUVEC TNF alpha + IFN gamma	34.6

Secondary Th1 rest	9.2	HUVEC TNF alpha + IL4	10.8
Secondary Th2 rest	12.9	HUVEC IL-11	14.2
Secondary Tr1 rest	18.9	Lung Microvascular EC none	36.3
Primary Th1 act	1.5	Lung Microvascular EC TNFalpha + IL-1beta	31.9
Primary Th2 act	7.2	Microvascular Dermal EC none	38.7
Primary Tr1 act	5.9	Microvascular Dermal EC TNFalpha + IL-1beta	16.4
Primary Th1 rest	56.6	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	41.8	Small airway epithelium none	2.3
Primary Tr1 rest	31.2	Small airway epithelium TNFalpha + IL-1beta	1.6
CD45RA CD4 lymphocyte act	4.4	Coronary artery SMC rest	5.4
CD45RO CD4 lymphocyte act	8.5	Coronary artery SMC TNFalpha + IL-1beta	0.9
CD8 lymphocyte act	3.6	Astrocytes rest	14.8
Secondary CD8 lymphocyte rest	5.3	Astrocytes TNFalpha + IL-1beta	3.4
Secondary CD8 lymphocyte act	6.9	KU-812 (Basophil) rest	0.3
CD4 lymphocyte none	8.1	KU-812 (Basophil) PMA/ionomycin	0.7
2ry Th1/Th2/Tr1_anti-CD95 CH11	20.0	CCD1106 (Keratinocytes) none	2.5
LAK cells rest	4.7	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	1.9
LAK cells IL-2	6.0	Liver cirrhosis	5.3
LAK cells IL-2+IL-12	11.8	Lupus kidney	1.6
LAK cells IL-2+IFN gamma	17.6	NCI-H292 none	1.8
LAK cells IL-2+ IL-18	19.3	NCI-H292 IL-4	0.2
LAK cells PMA/ionomycin	2.8	NCI-H292 IL-9	3.0
NK Cells IL-2 rest	22.8	NCI-H292 IL-13	0.4
Two Way MLR 3 day	21.2	NCI-H292 IFN gamma	2.5
Two Way MLR 5 day	7.7	HPAEC none	16.7
Two Way MLR 7 day	3.4	HPAEC TNF alpha + IL-1 beta	11.0
PBMC rest	1.1	Lung fibroblast none	9.9
PBMC PWM	15.7	Lung fibroblast TNF alpha + IL-1 beta	0.6
PBMC PHA-L	4.9	Lung fibroblast IL-4	5.6
Ramos (B cell) none	0.0	Lung fibroblast IL-9	9.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	8.1
B lymphocytes PWM	0.7	Lung fibroblast IFN gamma	10.4
B lymphocytes CD40L and IL-4	1.2	Dermal fibroblast CCD1070 rest	2.2
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	35.1
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	3.0
Dendritic cells none	0.2	Dermal fibroblast IFN gamma	3.9
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	10.7
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.9
Monocytes rest	0.0	IBD Crohn's	1.9
Monocytes LPS	11.5	Colon	7.2
Macrophages rest	8.0	Lung	0.0

Macrophages LPS	0.0	Thymus	12.4
HUVEC none	20.3	Kidney	100.0
HUVEC starved	82.4		

Table DE. Panel CNS_I

Tissue Name	Rel. Exp.(%) Ag3119, Run 182257490	Tissue Name	Rel. Exp.(%) Ag3119, Run 182257490
BA4 Control	2.8	BA17 PSP	2.6
BA4 Control2	0.0	BA17 PSP2	0.0
BA4 Alzheimer's2	2.2	Sub Nigra Control	1.3
BA4 Parkinson's	31.0	Sub Nigra Control2	11.3
BA4 Parkinson's2	7.2	Sub Nigra Alzheimer's2	5.7
BA4 Huntington's	26.8	Sub Nigra Parkinson's2	4.7
BA4 Huntington's2	5.9	Sub Nigra Huntington's	28.7
BA4 PSP	2.0	Sub Nigra Huntington's2	1.1
BA4 PSP2	4.6	Sub Nigra PSP2	0.0
BA4 Depression	14.5	Sub Nigra Depression	4.6
BA4 Depression2	6.8	Sub Nigra Depression2	0.0
BA7 Control	48.0	Glob Palladus Control	8.1
BA7 Control2	0.0	Glob Palladus Control2	8.2
BA7 Alzheimer's2	16.3	Glob Palladus Alzheimer's	6.1
BA7 Parkinson's	6.7	Glob Palladus Alzheimer's2	6.9
BA7 Parkinson's2	30.1	Glob Palladus Parkinson's	44.1
BA7 Huntington's	2.8	Glob Palladus Parkinson's2	19.6
BA7 Huntington's2	75.8	Glob Palladus PSP	0.0
BA7 PSP	2.4	Glob Palladus PSP2	0.0
BA7 PSP2	3.6	Glob Palladus Depression	0.0
BA7 Depression	36.3	Temp Pole Control	7.1
BA9 Control	3.3	Temp Pole Control2	2.5
BA9 Control2	23.7	Temp Pole Alzheimer's	6.4
BA9 Alzheimer's	8.4	Temp Pole Alzheimer's2	9.1
BA9 Alzheimer's2	9.2	Temp Pole Parkinson's	29.1
BA9 Parkinson's	22.5	Temp Pole Parkinson's2	2.8
BA9 Parkinson's2	10.4	Temp Pole Huntington's	28.5
BA9 Huntington's	20.3	Temp Pole PSP	8.2
BA9 Huntington's2	35.8	Temp Pole PSP2	0.0
BA9 PSP	5.9	Temp Pole Depression2	0.0
BA9 PSP2	0.0	Cing Gyr Control	18.4
BA9 Depression	0.0	Cing Gyr Control2	4.5
BA9 Depression2	0.0	Cing Gyr Alzheimer's	5.3
BA17 Control	60.7	Cing Gyr Alzheimer's2	15.5
BA17 Control2	31.0	Cing Gyr Parkinson's	3.6
BA17 Alzheimer's2	36.9	Cing Gyr Parkinson's2	30.6
BA17 Parkinson's	40.3	Cing Gyr Huntington's	1.6
BA17 Parkinson's2	100.0	Cing Gyr Huntington's2	1.6
BA17 Huntington's	1.8	Cing Gyr PSP	0.0
BA17 Huntington's2	37.1	Cing Gyr PSP2	14.5
BA17 Depression	7.2	Cing Gyr Depression	0.0
BA17 Depression2	4.3	Cing Gyr Depression2	5.8

5

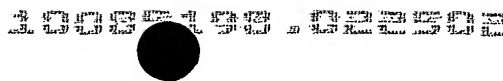
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catalyze the refolding of partly denatured proteins and stabilize multiprotein complexes such as Ca(2+) channels, inactive steroid receptor complexes, and receptor protein tyrosine kinases. Generally, these effects appear to depend on the ability of immunophilins to selectively bind to other proteins. This review will examine in detail experimental and structural investigations of the mechanism of PPIase activity for both FKBP and cyclophilins and suggest a mechanism for these enzymes, which depends on their ability to recognize a specific peptide conformation rather than sequence. Examination of structures of immunophilin-protein complexes will then be used to further suggest that the ability of these enzymes to recognize specific peptide conformations is central to the formation of these complexes and may constitute a general function of immunophilin enzymes. The binding of ligand to immunophilins will also be shown to stabilize specific conformations in surface loops of these proteins that are observed to play a critical role in a number of immunophilin-protein complexes suggesting that the immunophilins may constitute a class of ligand-triggered selective protein binders.

PMID: 11058892

2. Russell G, Graveley R, Seid J, al-Humidan AK, Skjodt H. Mechanisms of action of cyclosporine and effects on connective tissues. *Semin Arthritis Rheum* 1992 Jun;21(6 Suppl 3):16-22.

Cyclosporine is a potent immunomodulatory agent with an increasing number of clinical applications. Its major mode of action is inhibition of the production of cytokines involved in the regulation of T-cell activation. In particular, cyclosporine inhibits the transcription of interleukin 2. Although cyclosporine's major actions are on T cells, there is some evidence that it produces direct effects on other cell types. Its immunosuppressive action is closely linked to its binding of cyclophilin, a member of a family of high-affinity cyclosporine-binding proteins widely distributed in different cell types and in different species. The cyclophilins have been shown to have peptidyl-prolyl cis-trans isomerase enzyme activity that is blocked by cyclosporine. Although this may be a factor in cyclosporine's selective inhibition of cytokine gene transcription, it is still unclear whether inhibition of this activity is the mechanism through which cyclosporine exerts its effects on target cells. The ubiquitous presence of cyclophilins raises the question of why cyclosporine has major effects on T cells. Perhaps the critical proteins affected are transcriptional regulators restricted in their tissue distribution. The effects of cyclosporine on T cells and, directly or indirectly, on connective tissue cells, all of which can produce a range of cytokines, are of interest in relation to the tissue changes that occur in such inflammatory conditions as rheumatoid arthritis.

PMID: 1502562

Panel 4D Summary: Ag3119 The CG57149-01 gene is expressed at moderate levels in T cells and is also expressed at significant levels in endothelium, epithelium and fibroblasts as well as in normal thymus and kidney. Expression of this gene in thymus is consistent with what is observed in Panel 1.3D. Furthermore, treatment of proinflammatory mediators reduces the level of this transcript in HUVEC cells as compared to in starved cells. The protein encoded for by this transcript may be important in the normal function of the cell types that express it. Regulation of the protein encoded for by this transcript could be important for maintaining or resuming normal homeostasis.

Panel CNS_1 Summary: Ag3119 This panel confirms the expression of this gene at low levels in the brain in an independent group of individuals. Please see Panel 1.3D for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

NOV37

Expression of NOV37/CG57151-01 was assessed using the primer-probe set Ag3120, described in Table AEA. Results of the RTQ-PCR runs are shown in Tables AEB, AEC, AED and AEE.

Table AEA. Probe Name Ag3120

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-atgctctgagcactggagaa-3'	20	215	368
Probe	TET-5'-tcctgctttcacagaattattccaggg-3'-TAMRA	27	256	369
Reverse	5'-gtgtgaagtcaccactctgaca-3'	22	289	370

Table AEB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3120, Run 208976883	Tissue Name	Rel. Exp.(%) Ag3120, Run 208976883
AD 1 Hippo	18.6	Control (Path) 3 Temporal Ctx	6.2
AD 2 Hippo	26.1	Control (Path) 4 Temporal Ctx	46.0
AD 3 Hippo	10.1	AD 1 Occipital Ctx	26.4
AD 4 Hippo	10.2	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	90.1	AD 3 Occipital Ctx	8.9
AD 6 Hippo	67.8	AD 4 Occipital Ctx	24.5
Control 2 Hippo	35.1	AD 5 Occipital Ctx	47.3
Control 4 Hippo	16.8	AD 6 Occipital Ctx	36.6
Control (Path) 3 Hippo	12.0	Control 1 Occipital Ctx	6.5
AD 1 Temporal Ctx	35.8	Control 2 Occipital Ctx	74.7
AD 2 Temporal Ctx	41.5	Control 3 Occipital Ctx	36.6
AD 3 Temporal Ctx	10.3	Control 4 Occipital Ctx	8.7
AD 4 Temporal Ctx	25.0	Control (Path) 1 Occipital	100.0

		Ctx	
AD 5 Inf Temporal Ctx	87.1	Control (Path) 2 Occipital Ctx	17.1
AD 5 Sup Temporal Ctx	57.8	Control (Path) 3 Occipital Ctx	5.1
AD 6 Inf Temporal Ctx	79.6	Control (Path) 4 Occipital Ctx	37.9
AD 6 Sup Temporal Ctx	97.9	Control 1 Parietal Ctx	13.1
Control 1 Temporal Ctx	12.2	Control 2 Parietal Ctx	44.8
Control 2 Temporal Ctx	43.2	Control 3 Parietal Ctx	19.5
Control 3 Temporal Ctx	26.6	Control (Path) 1 Parietal Ctx	65.5
Control 4 Temporal Ctx	13.5	Control (Path) 2 Parietal Ctx	40.6
Control (Path) 1 Temporal Ctx	59.5	Control (Path) 3 Parietal Ctx	3.9
Control (Path) 2 Temporal Ctx	47.3	Control (Path) 4 Parietal Ctx	56.3

Table AEC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag3120, Run 167985266	Tissue Name	Rel. Exp.(%) Ag3120, Run 167985266
Liver adenocarcinoma	46.0	Kidney (fetal)	97.3
Pancreas	14.3	Renal ca. 786-0	25.7
Pancreatic ca. CAPAN 2	8.2	Renal ca. A498	26.2
Adrenal gland	12.8	Renal ca. RXF 393	43.5
Thyroid	8.4	Renal ca. ACHN	12.0
Salivary gland	3.2	Renal ca. UO-31	29.5
Pituitary gland	16.8	Renal ca. TK-10	36.9
Brain (fetal)	30.1	Liver	8.7
Brain (whole)	12.4	Liver (fetal)	18.7
Brain (amygdala)	20.0	Liver ca. (hepatoblast) HepG2	42.0
Brain (cerebellum)	30.8	Lung	12.2
Brain (hippocampus)	16.4	Lung (fetal)	45.7
Brain (substantia nigra)	42.3	Lung ca. (small cell) LX-1	26.2
Brain (thalamus)	3.0	Lung ca. (small cell) NCI-H69	10.1
Cerebral Cortex	12.4	Lung ca. (s.cell var.) SHP-77	85.3
Spinal cord	24.5	Lung ca. (large cell) NCI-H460	4.2
glio/astro U87-MG	20.4	Lung ca. (non-sm. cell) A549	32.5
glio/astro U-118-MG	24.7	Lung ca. (non-s.cell) NCI-H23	26.4
astrocytoma SW1783	16.5	Lung ca. (non-s.cell) HOP-62	15.0
neuro*; met SK-N-AS	21.9	Lung ca. (non-s.cl) NCI-H522	15.6
astrocytoma SF-539	21.6	Lung ca. (squam.) SW 900	26.8
astrocytoma SNB-75	28.3	Lung ca. (squam.) NCI-H596	33.7
glioma SNB-19	12.8	Mammary gland	6.7
glioma U251	47.0	Breast ca.* (pl.ef) MCF-7	26.1
glioma SF-295	13.3	Breast ca.* (pl.ef) MDA-MB-231	22.7

Heart (fetal)	8.7	Breast ca. * (pl.ef) T47D	43.5
Heart	11.6	Breast ca. BT-549	16.4
Skeletal muscle (fetal)	5.4	Breast ca. MDA-N	25.0
Skeletal muscle	10.8	Ovary	5.2
Bone marrow	26.4	Ovarian ca. OVCAR-3	13.5
Thymus	49.7	Ovarian ca. OVCAR-4	21.3
Spleen	49.7	Ovarian ca. OVCAR-5	100.0
Lymph node	37.4	Ovarian ca. OVCAR-8	6.8
Colorectal	7.3	Ovarian ca. IGROV-1	8.0
Stomach	12.7	Ovarian ca. * (ascites) SK-OV-3	56.3
Small intestine	14.6	Uterus	16.7
Colon ca. SW480	29.5	Placenta	5.1
Colon ca.* SW620(SW480 met)	52.1	Prostate	11.1
Colon ca. HT29	23.0	Prostate ca.* (bone met)PC-3	22.2
Colon ca. HCT-116	23.8	Testis	8.4
Colon ca. CaCo-2	48.0	Melanoma Hs688(A).T	4.5
Colon ca. tissue(ODO3866)	32.5	Melanoma* (met) Hs688(B).T	4.1
Colon ca. HCC-2998	32.5	Melanoma UACC-62	13.0
Gastric ca. * (liver met) NCI-N87	27.4	Melanoma M14	11.0
Bladder	34.2	Melanoma LOX IMVI	15.4
Trachea	12.3	Melanoma * (met) SK-MEL-5	12.6
Kidney	22.7	Adipose	44.4

Table AED. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3120, Run 164526129	Tissue Name	Rel. Exp.(%) Ag3120, Run 164526129
Secondary Th1 act	15.5	HUVEC IL-1beta	7.1
Secondary Th2 act	17.6	HUVEC IFN gamma	19.3
Secondary Tr1 act	21.0	HUVEC TNF alpha + IFN gamma	12.4
Secondary Th1 rest	9.0	HUVEC TNF alpha + IL4	16.0
Secondary Th2 rest	10.7	HUVEC IL-11	20.7
Secondary Tr1 rest	16.8	Lung Microvascular EC none	12.1
Primary Th1 act	17.3	Lung Microvascular EC TNFalpha + IL-1beta	11.9
Primary Th2 act	15.7	Microvascular Dermal EC none	14.0
Primary Tr1 act	23.8	Microvascular Dermal EC TNFalpha + IL-1beta	7.6
Primary Th1 rest	50.0	Bronchial epithelium TNFalpha + IL1beta	18.0
Primary Th2 rest	33.2	Small airway epithelium none	7.0
Primary Tr1 rest	26.8	Small airway epithelium TNFalpha + IL-1beta	34.4
CD45RA CD4 lymphocyte act	9.8	Coronary artery SMC rest	8.1
CD45RO CD4 lymphocyte act	21.3	Coronary artery SMC TNFalpha + IL-1beta	5.0
CD8 lymphocyte act	23.7	Astrocytes rest	4.9
Secondary CD8 lymphocyte rest	23.2	Astrocytes TNFalpha + IL-1beta	7.0
Secondary CD8 lymphocyte act	10.2	KU-812 (Basophil) rest	8.3

BA7 Parkinson's	26.8	Glob Palladus Alzheimer's2	12.8
BA7 Parkinson's2	49.3	Glob Palladus Parkinson's	95.9
BA7 Huntington's	50.7	Glob Palladus Parkinson's2	15.4
BA7 Huntington's2	66.4	Glob Palladus PSP	12.9
BA7 PSP	70.7	Glob Palladus PSP2	10.1
BA7 PSP2	23.7	Glob Palladus Depression	7.3
BA7 Depression	24.1	Temp Pole Control	14.9
BA9 Control	16.7	Temp Pole Control2	39.2
BA9 Control2	78.5	Temp Pole Alzheimer's	10.5
BA9 Alzheimer's	11.2	Temp Pole Alzheimer's2	11.4
BA9 Alzheimer's2	38.7	Temp Pole Parkinson's	30.8
BA9 Parkinson's	33.2	Temp Pole Parkinson's2	40.3
BA9 Parkinson's2	88.3	Temp Pole Huntington's	65.5
BA9 Huntington's	37.6	Temp Pole PSP	3.3
BA9 Huntington's2	20.4	Temp Pole PSP2	7.6
BA9 PSP	23.3	Temp Pole Depression2	18.8
BA9 PSP2	2.7	Cing Gyr Control	47.6
BA9 Depression	13.0	Cing Gyr Control2	26.1
BA9 Depression2	12.1	Cing Gyr Alzheimer's	22.2
BA17 Control	88.3	Cing Gyr Alzheimer's2	23.0
BA17 Control2	82.9	Cing Gyr Parkinson's	43.2
BA17 Alzheimer's2	35.1	Cing Gyr Parkinson's2	37.4
BA17 Parkinson's	99.3	Cing Gyr Huntington's	60.3
BA17 Parkinson's2	100.0	Cing Gyr Huntington's2	39.8
BA17 Huntington's	45.7	Cing Gyr PSP	38.2
BA17 Huntington's2	40.3	Cing Gyr PSP2	10.2
BA17 Depression	38.7	Cing Gyr Depression	21.5
BA17 Depression2	48.3	Cing Gyr Depression2	16.7

CNS_neurodegeneration_v1.0 Summary: Ag3120 This panel confirms the expression of this gene at moderate levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.3D for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

Panel 1.3D Summary: Ag3120 The CG57151-01 gene is expressed at moderate to low levels in all tissues on this panel, with the highest expression seen in ovarian cancer cell line OVCAR-5 (CT = 29.1). This gene is expressed at moderate levels throughout the central nervous system, including in amygdala, hippocampus, cerebral cortex, cerebellum, substantia nigra, and spinal cord, with lower expression detected in thalamus. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

Among tissues with metabolic or endocrine function, this gene is expressed at low to moderate levels in adrenal gland, thyroid, pituitary gland, pancreas, adipose, skeletal muscle, heart and liver. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine and metabolically related diseases, such as obesity and diabetes.

This gene encodes a protein with homology to peptidyl-prolyl cis/trans isomerase A (PPIA or cyclophilin A), a cytosolic enzyme involved in protein folding and/or intracellular protein transport. Cyclophilin genes are expressed in numerous tissues. The interaction of cyclophilin and cyclosporine has an effect on cytokine production in T-cells. Therefore, modulation of this gene may be used in the treatment of inflammatory diseases such as rheumatoid arthritis.

References:

1. Russell G, Graveley R, Seid J, al-Humidan AK, Skjodt H. Mechanisms of action of cyclosporine and effects on connective tissues. *Semin Arthritis Rheum* 1992 Jun;21(6 Suppl 3):16-22.

Cyclosporine is a potent immunomodulatory agent with an increasing number of clinical applications. Its major mode of action is inhibition of the production of cytokines involved in the regulation of T-cell activation. In particular, cyclosporine inhibits the transcription of interleukin 2. Although cyclosporine's major actions are on T cells, there is some evidence that it produces direct effects on other cell types. Its immunosuppressive action is closely linked to its binding of cyclophilin, a member of a family of high-affinity cyclosporine-binding proteins widely distributed in different cell types and in different species. The cyclophilins have been shown to have peptidyl-prolyl cis-trans isomerase enzyme activity that is blocked by cyclosporine. Although this may be a factor in cyclosporine's selective inhibition of cytokine gene transcription, it is still unclear whether inhibition of this activity is the mechanism through which cyclosporine exerts its effects on target cells. The ubiquitous presence of cyclophilins raises the question of why cyclosporine has major effects on T cells. Perhaps the critical proteins affected are transcriptional regulators restricted in their tissue distribution. The effects of cyclosporine on T cells and, directly or indirectly, on connective tissue cells, all of which can produce a range of cytokines, are of interest in relation to the tissue changes that occur in such inflammatory conditions as rheumatoid arthritis.

PMID: 1502562

Panel 4D Summary: Ag3120 The CG57151-01 gene is expressed at high to moderate levels in a wide range of cell types of significance in the immune response in health and

disease. These cells include members of the T-cell, B-cell, endothelial cell, macrophage/monocyte/dendritic cell, basophil, eosinophil, and peripheral blood mononuclear cell family, as well as epithelial and fibroblast cell types from lung and skin, and normal tissues represented by colon, lung, thymus and kidney. This ubiquitous pattern of expression suggests that this gene product may be involved in homeostatic processes for these and other cell types and tissues.

This pattern is in agreement with the expression profile in Panel 1.3D and also suggests a role for the gene product in cell survival and proliferation.

Panel CNS_1 Summary: Ag3120 This panel confirms the expression of this gene at low to moderate levels in the brain in an independent group of individuals. Please see Panel 1.3D for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

NOV38

Expression of NOV38/CG57153-01 was assessed using the primer-probe set Ag3121,
described in Table AFA. Results of the RTQ-PCR runs are shown in Tables AFB, AFC, AFD
and AFE.

Table AFA. Probe Name Ag3121

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-tccagggtttatatgccagagt-3'	22	249	371
Probe	TET-5'-cacatgtcatgatgacactggcacaa-3'-TAMRA	26	279	372
Reverse	5'-cagacttctccagtagttgga-3'	22	307	373

Table AFB. CNS neurodegeneration v1.0

Tissue Name	Rel. Exp.(%) Ag3121, Run 208976899	Tissue Name	Rel. Exp.(%) Ag3121, Run 208976899
AD 1 Hippo	0.0	Control (Path) 3 Temporal Ctx	3.5
AD 2 Hippo	100.0	Control (Path) 4 Temporal Ctx	33.2
AD 3 Hippo	0.0	AD 1 Occipital Ctx	13.4
AD 4 Hippo	15.4	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	5.0	AD 3 Occipital Ctx	0.0

AD 6 Hippo	66.4	AD 4 Occipital Ctx	7.7
Control 2 Hippo	32.5	AD 5 Occipital Ctx	3.8
Control 4 Hippo	17.8	AD 6 Occipital Ctx	3.1
Control (Path) 3 Hippo	0.0	Control 1 Occipital Ctx	0.0
AD 1 Temporal Ctx	0.0	Control 2 Occipital Ctx	0.0
AD 2 Temporal Ctx	18.0	Control 3 Occipital Ctx	0.0
AD 3 Temporal Ctx	0.0	Control 4 Occipital Ctx	0.0
AD 4 Temporal Ctx	14.0	Control (Path) 1 Occipital Ctx	6.5
AD 5 Inf Temporal Ctx	28.3	Control (Path) 2 Occipital Ctx	12.7
AD 5 Sup Temporal Ctx	37.4	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	10.8	Control (Path) 4 Occipital Ctx	0.0
AD 6 Sup Temporal Ctx	35.1	Control 1 Parietal Ctx	0.0
Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	35.4
Control 2 Temporal Ctx	5.2	Control 3 Parietal Ctx	6.4
Control 3 Temporal Ctx	13.2	Control (Path) 1 Parietal Ctx	14.5
Control 3 Temporal Ctx	0.0	Control (Path) 2 Parietal Ctx	6.4
Control (Path) 1 Temporal Ctx	19.8	Control (Path) 3 Parietal Ctx	0.0
Control (Path) 2 Temporal Ctx	28.9	Control (Path) 4 Parietal Ctx	6.5

Table AFC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag3121, Run 167985269	Tissue Name	Rel. Exp.(%) Ag3121, Run 167985269
Liver adenocarcinoma	0.0	Kidney (fetal)	9.3
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	3.3	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	100.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	6.3	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	11.3	Lung (fetal)	0.0
Brain (substantia nigra)	3.1	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	0.0	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	0.0	Lung ca. (large cell) NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	6.3	Lung ca. (non-s.cl) NCI-	0.0

		H522	
astrocytoma SF-539	0.0	Lung ca. (squamous) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squamous) NCI-H596	0.0
glioma SNB-19	3.1	Mammary gland	0.0
glioma U251	4.8	Breast ca. * (pl. ef) MCF-7	0.0
glioma SF-295	0.0	Breast ca. * (pl. ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca. * (pl. ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	0.0
Lymph node	0.0	Ovarian ca. OVCAR-8	2.5
Colorectal	0.0	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca. * (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Placenta	0.0
Colon ca. * SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca. * (bone met) PC-3	0.0
Colon ca. HCT-116	0.0	Testis	0.0
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	4.7	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca. * (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table AFD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3121, Run 164526517	Tissue Name	Rel. Exp.(%) Ag3121, Run 164526517
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	9.7
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	33.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0

CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	100.0
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	10.9
PBMC PHA-L	0.0	Lung fibroblast IL-4	22.2
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	37.6
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	28.9
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Table AFE. Panel CNS_1

Tissue Name	Rel. Exp.(%) Ag3121, Run 171694170	Rel. Exp.(%) Ag3121, Run 182257570	Tissue Name	Rel. Exp.(%) Ag3121, Run 171694170	Rel. Exp.(%) Ag3121, Run 182257570
BA4 Control	24.0	57.0	BA17 PSP	0.0	0.0
BA4 Control2	49.0	0.0	BA17 PSP2	0.0	0.0
BA4 Alzheimer's2	0.0	33.2	Sub Nigra Control	0.0	25.0
BA4 Parkinson's	33.0	72.7	Sub Nigra Control2	0.0	0.0

BA4 Parkinson's2	0.0	27.9	Sub Nigra Alzheimer's2	27.9	0.0
BA4 Huntington's	11.4	0.0	Sub Nigra Parkinson's2	0.0	0.0
BA4 Huntington's2	0.0	0.0	Sub Nigra Huntington's	0.0	82.9
BA4 PSP	0.0	21.8	Sub Nigra Huntington's2	0.0	0.0
BA4 PSP2	26.8	0.0	Sub Nigra PSP2	0.0	0.0
BA4 Depression	8.1	30.1	Sub Nigra Depression	0.0	0.0
BA4 Depression2	0.0	0.0	Sub Nigra Depression2	0.0	0.0
BA7 Control	0.0	0.0	Glob Palladus Control	0.0	0.0
BA7 Control2	29.3	0.0	Glob Palladus Control2	0.0	0.0
BA7 Alzheimer's2	0.0	0.0	Glob Palladus Alzheimer's	24.8	0.0
BA7 Parkinson's	0.0	0.0	Glob Palladus Alzheimer's2	0.0	0.0
BA7 Parkinson's2	0.0	0.0	Glob Palladus Parkinson's	82.4	58.2
BA7 Huntington's	29.7	19.9	Glob Palladus Parkinson's2	27.4	0.0
BA7 Huntington's2	28.5	0.0	Glob Palladus PSP	0.0	24.1
BA7 PSP	0.0	0.0	Glob Palladus PSP2	0.0	0.0
BA7 PSP2	0.0	0.0	Glob Palladus Depression	0.0	26.8
BA7 Depression	0.0	0.0	Temp Pole Control	21.3	33.0
BA9 Control	0.0	0.0	Temp Pole Control2	27.7	0.0
BA9 Control2	100.0	36.1	Temp Pole Alzheimer's	0.0	0.0
BA9 Alzheimer's	0.0	0.0	Temp Pole Alzheimer's2	0.0	0.0
BA9 Alzheimer's2	24.7	0.0	Temp Pole Parkinson's	0.0	31.6
BA9 Parkinson's	0.0	26.2	Temp Pole Parkinson's2	50.3	0.0
BA9 Parkinson's2	0.0	30.6	Temp Pole Huntington's	0.0	0.0
BA9 Huntington's	0.0	0.0	Temp Pole PSP	0.0	0.0
BA9 Huntington's2	0.0	29.1	Temp Pole PSP2	0.0	0.0
BA9 PSP	0.0	100.0	Temp Pole Depression2	0.0	0.0
BA9 PSP2	0.0	0.0	Cing Gyr Control	0.0	94.6
BA9 Depression	0.0	0.0	Cing Gyr Control2	0.0	30.8
BA9 Depression2	0.0	0.0	Cing Gyr Alzheimer's	0.0	0.0
BA17 Control	0.0	37.9	Cing Gyr Alzheimer's2	0.0	0.0
BA17 Control2	45.1	0.0	Cing Gyr	28.3	29.3

			Parkinson's		
BA17 Alzheimer's2	0.0	0.0	Cing Gyr Parkinson's2	0.0	91.4
BA17 Parkinson's	0.0	27.7	Cing Gyr Huntington's	14.2	28.7
BA17 Parkinson's2	0.0	43.8	Cing Gyr Huntington's2	90.1	41.8
BA17 Huntington's	24.8	0.0	Cing Gyr PSP	28.1	29.9
BA17 Huntington's2	0.0	0.0	Cing Gyr PSP2	0.0	0.0
BA17 Depression	0.0	0.0	Cing Gyr Depression	0.0	31.2
BA17 Depression2	0.0	29.1	Cing Gyr Depression2	0.0	0.0

CNS_neurodegeneration_v1.0 Summary: Ag3121 This panel confirms the expression of this gene at low levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.3D for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

Panel 1.3D Summary: Ag3121 Significant expression of the CG57153-01 gene is restricted to a sample derived from fetal brain tissue (CT = 33.1). Interestingly, expression of this gene is much lower in adult brain (CT = 40), suggesting that expression of this gene can be used to distinguish fetal brain from adult brain as well as the other samples on this panel. In addition, the relative overexpression of this gene in fetal brain suggests that the protein product may enhance brain development in the fetus and thus may also act in a regenerative capacity in the adult. Therefore, therapeutic modulation of the cyclophilin encoded by this gene could be useful in treatment of neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease.

Panel 4D Summary: Ag3121 Significant expression of this gene is detected in a liver cirrhosis sample (CT = 33.64). Furthermore, expression of this gene is not detected in normal liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative cyclophilin; therefore, small molecule therapeutics designed against this protein could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this protein could also be used for the diagnosis of liver cirrhosis.

Panel CNS_1 Summary: Ag3121 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV39

Expression of NOV39./G57155-01 was assessed using the primer-probe set Ag3122, described in Table AGA. Results of the RTQ-PCR runs are shown in Tables AGB, AGC, AGD and AGE.

5 Table AGA. Probe Name Ag3122

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-agcaacgggtcacaattctata-3'	22	355	374
Probe	TET-5'-tcacactgcaagcaactccttctaga-3'-TAMRA	28	377	375
Reverse	5'-atacccaaaagccacaaatttt-3'	22	408	376

Table AGB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3122, Run 208976900	Tissue Name	Rel. Exp.(%) Ag3122, Run 208976900
AD 1 Hippo	30.4	Control (Path) 3 Temporal Ctx	9.7
AD 2 Hippo	33.4	Control (Path) 4 Temporal Ctx	28.5
AD 3 Hippo	22.1	AD 1 Occipital Ctx	12.2
AD 4 Hippo	10.2	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	100.0	AD 3 Occipital Ctx	11.7
AD 6 Hippo	59.5	AD 4 Occipital Ctx	16.2
Control 2 Hippo	33.4	AD 5 Occipital Ctx	22.5
Control 4 Hippo	27.9	AD 6 Occipital Ctx	48.6
Control (Path) 3 Hippo	14.9	Control 1 Occipital Ctx	3.1
AD 1 Temporal Ctx	23.0	Control 2 Occipital Ctx	42.6
AD 2 Temporal Ctx	0.0	Control 3 Occipital Ctx	17.6
AD 3 Temporal Ctx	10.4	Control 4 Occipital Ctx	12.6
AD 4 Temporal Ctx	22.5	Control (Path) 1 Occipital Ctx	83.5
AD 5 Inf Temporal Ctx	86.5	Control (Path) 2 Occipital Ctx	13.4
AD 5 SupTemporal Ctx	57.8	Control (Path) 3 Occipital Ctx	4.9
AD 6 Inf Temporal Ctx	55.1	Control (Path) 4 Occipital Ctx	12.2
AD 6 Sup Temporal Ctx	80.7	Control 1 Parietal Ctx	6.5
Control 1 Temporal Ctx	5.9	Control 2 Parietal Ctx	45.7
Control 2 Temporal Ctx	43.8	Control 3 Parietal Ctx	22.5
Control 3 Temporal Ctx	14.0	Control (Path) 1 Parietal Ctx	64.6
Control 4 Temporal Ctx	10.1	Control (Path) 2 Parietal Ctx	31.9
Control (Path) 1 Temporal Ctx	73.2	Control (Path) 3 Parietal Ctx	11.0
Control (Path) 2 Temporal Ctx	33.7	Control (Path) 4 Parietal Ctx	48.3

Table AGC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag3122, Run 167985270	Tissue Name	Rel. Exp.(%) Ag3122, Run 167985270
Liver adenocarcinoma	5.7	Kidney (fetal)	100.0

Pancreas	13.2	Renal ca. 786-0	20.6
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	22.5
Adrenal gland	0.0	Renal ca. RXF 393	22.1
Thyroid	40.1	Renal ca. ACHN	28.3
Salivary gland	0.0	Renal ca. UO-31	5.0
Pituitary gland	19.1	Renal ca. TK-10	9.5
Brain (fetal)	88.9	Liver	0.0
Brain (whole)	11.0	Liver (fetal)	0.0
Brain (amygdala)	73.7	Liver ca. (hepatoblast) HepG2	7.2
Brain (cerebellum)	45.7	Lung	8.5
Brain (hippocampus)	33.0	Lung (fetal)	77.4
Brain (substantia nigra)	27.7	Lung ca. (small cell) LX-1	23.5
Brain (thalamus)	11.5	Lung ca. (small cell) NCI-H69	20.6
Cerebral Cortex	12.2	Lung ca. (s.cell var.) SHP-77	56.6
Spinal cord	55.9	Lung ca. (large cell) NCI-H460	0.0
glio/astro U87-MG	9.7	Lung ca. (non-sm. cell) A549	34.9
glio/astro U-118-MG	2.5	Lung ca. (non-s.cell) NCI-H23	40.3
astrocytoma SW1783	3.5	Lung ca. (non-s.cell) HOP-62	8.4
neuro*; met SK-N-AS	6.1	Lung ca. (non-s.cl) NCI-H522	33.2
astrocytoma SF-539	5.3	Lung ca. (squam.) SW 900	14.9
astrocytoma SNB-75	12.2	Lung ca. (squam.) NCI-H596	39.8
glioma SNB-19	11.3	Mammary gland	0.0
glioma U251	13.1	Breast ca.* (pl.ef) MCF-7	0.0
glioma SF-295	36.1	Breast ca.* (pl.ef) MDA-MB-231	6.9
Heart (fetal)	20.6	Breast ca.* (pl.ef) T47D	77.9
Heart	0.0	Breast ca. BT-549	3.7
Skeletal muscle (fetal)	14.5	Breast ca. MDA-N	2.8
Skeletal muscle	22.2	Ovary	13.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	12.0
Thymus	12.5	Ovarian ca. OVCAR-4	6.9
Spleen	3.6	Ovarian ca. OVCAR-5	29.3
Lymph node	17.8	Ovarian ca. OVCAR-8	2.7
Colorectal	4.9	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	39.8
Small intestine	6.2	Uterus	18.4
Colon ca. SW480	0.0	Placenta	0.0
Colon ca.* SW620(SW480 met)	13.0	Prostate	4.1
Colon ca. HT29	5.1	Prostate ca.* (bone met) PC-3	8.4
Colon ca. HCT-116	0.0	Testis	73.7
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	17.3	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	25.7	Melanoma UACC-62	2.1

Gastric ca.* (liver met) NCI-N87	35.4	Melanoma M14	5.6
Bladder	14.2	Melanoma LOX IMVI	0.0
Trachea	57.4	Melanoma* (met) SK-MEL-5	0.0
Kidney	59.0	Adipose	3.6

Table AGD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3122, Run 164527262	Tissue Name	Rel. Exp.(%) Ag3122, Run 164527262
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	1.4	HUVEC IFN gamma	3.1
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	3.8
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	1.1
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	3.2
Primary Th1 act	1.6	Lung Microvascular EC TNFalpha + IL-1beta	2.2
Primary Th2 act	3.1	Microvascular Dermal EC none	0.4
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	1.6
Primary Th1 rest	1.4	Bronchial epithelium TNFalpha + IL1beta	10.4
Primary Th2 rest	0.0	Small airway epithelium none	2.1
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	7.4
CD45RA CD4 lymphocyte act	0.5	Coronary artery SMC rest	1.5
CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	0.8
CD8 lymphocyte act	1.9	Astrocytes rest	6.3
Secondary CD8 lymphocyte rest	3.3	Astrocytes TNFalpha + IL-1beta	3.3
Secondary CD8 lymphocyte act	1.8	KU-812 (Basophil) rest	7.9
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	15.5
2ry Th1/Th2/Tr1_anti-CD95 CH11	1.5	CCD1106 (Keratinocytes) none	1.4
LAK cells rest	0.8	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.6	Liver cirrhosis	2.9
LAK cells IL-2+IL-12	4.5	Lupus kidney	2.2
LAK cells IL-2+IFN gamma	1.9	NCI-H292 none	4.1
LAK cells IL-2+ IL-18	2.0	NCI-H292 IL-4	4.8
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	9.9
NK Cells IL-2 rest	100.0	NCI-H292 IL-13	4.5
Two Way MLR 3 day	7.7	NCI-H292 IFN gamma	1.6
Two Way MLR 5 day	0.0	HPAEC none	0.6
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	1.0
PBMC rest	2.8	Lung fibroblast none	3.2
PBMC PWM	4.5	Lung fibroblast TNF alpha + IL-1 beta	1.4
PBMC PHA-L	0.9	Lung fibroblast IL-4	5.8
Ramos (B cell) none	0.0	Lung fibroblast IL-9	1.1
Ramos (B cell) ionomycin	8.0	Lung fibroblast IL-13	3.8
B lymphocytes PWM	9.2	Lung fibroblast IFN gamma	13.8

B lymphocytes CD40L and IL-4	2.5	Dermal fibroblast CCD1070 rest	1.2
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	3.2
EOL-1 dbcAMP PMA/ionomycin	3.0	Dermal fibroblast CCD1070 IL-1 beta	2.5
Dendritic cells none	1.0	Dermal fibroblast IFN gamma	1.2
Dendritic cells LPS	2.5	Dermal fibroblast IL-4	5.8
Dendritic cells anti-CD40	0.7	IBD Colitis 2	1.4
Monocytes rest	1.6	IBD Crohn's	3.2
Monocytes LPS	1.4	Colon	4.8
Macrophages rest	2.9	Lung	11.9
Macrophages LPS	0.0	Thymus	59.9
HUVEC none	0.0	Kidney	6.1
HUVEC starved	1.3		

Table AGE. Panel CNS_1

Tissue Name	Rel. Exp.(%) Ag3122, Run 182257573	Tissue Name	Rel. Exp.(%) Ag3122, Run 182257573
BA4 Control	47.0	BA17 PSP	19.1
BA4 Control2	81.2	BA17 PSP2	9.2
BA4 Alzheimer's2	0.0	Sub Nigra Control	27.7
BA4 Parkinson's	53.6	Sub Nigra Control2	14.2
BA4 Parkinson's2	72.7	Sub Nigra Alzheimer's2	16.4
BA4 Huntington's	47.0	Sub Nigra Parkinson's2	24.0
BA4 Huntington's2	8.2	Sub Nigra Huntington's	100.0
BA4 PSP	7.7	Sub Nigra Huntington's2	36.1
BA4 PSP2	7.5	Sub Nigra PSP2	15.9
BA4 Depression	24.3	Sub Nigra Depression	16.3
BA4 Depression2	15.3	Sub Nigra Depression2	0.0
BA7 Control	29.5	Glob Palladus Control	18.2
BA7 Control2	24.5	Glob Palladus Control2	99.3
BA7 Alzheimer's2	24.0	Glob Palladus Alzheimer's	0.0
BA7 Parkinson's	20.9	Glob Palladus Alzheimer's2	8.7
BA7 Parkinson's2	29.3	Glob Palladus Parkinson's	100.0
BA7 Huntington's	31.9	Glob Palladus Parkinson's2	15.8
BA7 Huntington's2	68.8	Glob Palladus PSP	7.2
BA7 PSP	11.0	Glob Palladus PSP2	0.0
BA7 PSP2	7.5	Glob Palladus Depression	9.7
BA7 Depression	11.3	Temp Pole Control	12.3
BA9 Control	24.3	Temp Pole Control2	32.5
BA9 Control2	44.4	Temp Pole Alzheimer's	11.9
BA9 Alzheimer's	8.8	Temp Pole Alzheimer's2	0.0
BA9 Alzheimer's2	19.3	Temp Pole Parkinson's	37.1
BA9 Parkinson's	28.5	Temp Pole Parkinson's2	30.1
BA9 Parkinson's2	30.4	Temp Pole Huntington's	28.1
BA9 Huntington's	54.7	Temp Pole PSP	14.7
BA9 Huntington's2	17.4	Temp Pole PSP2	0.0
BA9 PSP	0.0	Temp Pole Depression2	19.8
BA9 PSP2	7.4	Cing Gyr Control	49.0
BA9 Depression	12.6	Cing Gyr Control2	19.3
BA9 Depression2	0.0	Cing Gyr Alzheimer's	11.0
BA17 Control	50.7	Cing Gyr Alzheimer's2	6.3

BA17 Control2	35.8	Cing Gyr Parkinson's	39.8
BA17 Alzheimer's2	9.0	Cing Gyr Parkinson's2	31.6
BA17 Parkinson's	38.4	Cing Gyr Huntington's	59.5
BA17 Parkinson's2	60.7	Cing Gyr Huntington's2	13.5
BA17 Huntington's	19.6	Cing Gyr PSP	26.4
BA17 Huntington's2	34.4	Cing Gyr PSP2	0.0
BA17 Depression	14.4	Cing Gyr Depression	0.0
BA17 Depression2	24.0	Cing Gyr Depression2	12.5

CNS_neurodegeneration_v1.0 Summary: Ag3122 This panel confirms the expression of this gene at low levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.3D for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

Panel 1.3D Summary: Ag3122 Expression of the CG57155-01 gene is highest in fetal kidney (CT = 34.3). In addition, low but significant expression of this gene is detected in fetal brain (CT = 34.5) and fetal lung (CT = 34.6). Interestingly, expression of the CG57155-01 gene is much lower in adult brain (CT = 37.5) and adult lung (CT = 37.8). This observation suggests that expression of this gene can be used to distinguish fetal brain from adult brain as well as fetal lung from adult lung. In addition, the relative overexpression of this gene in fetal brain suggests that the protein product may enhance brain development in the fetus and thus may also act in a regenerative capacity in the adult. Therefore, therapeutic modulation of the cyclophilin encoded by this gene could be useful in treatment of neurodegenerative diseases.

Panel 4D Summary: Ag3122 Expression of the CG57155-01 gene is highest in natural killer cells (CT = 31). This observation suggests that therapeutic modulation of this gene using small molecule drugs could be of use in the treatment of viral or bacterial intracellular infections.

In addition, this gene is expressed at significant levels in thymus (CT = 31.8). The putative cyclophilin encoded for by the CG57155-01 gene could therefore play an important role in T cell development. Small molecule therapeutics, or antibody therapeutics designed against the protein encoded for by this gene could be utilized to modulate immune function (T cell development) and be important for organ transplant, AIDS treatment or post chemotherapy immune reconstitution.

This gene encodes a protein with homology to peptidyl-prolyl cis/trans isomerase A (PPIA or cyclophilin A), a cytosolic enzyme involved in protein folding and/or intracellular

protein transport. Cyclophilin genes have been shown to be expressed in numerous tissues. The interaction of cyclophilin and cyclosporine has an effect on cytokine production in T-cells. Therefore, modulation of this gene may be used in the treatment of inflammatory diseases such as rheumatoid arthritis.

5 References:

1. Russell G, Graveley R, Seid J, al-Humidan AK, Skjodt H. Mechanisms of action of cyclosporine and effects on connective tissues. Semin Arthritis Rheum 1992 Jun;21(6 Suppl 3):16-22.

10 Cyclosporine is a potent immunomodulatory agent with an increasing number of clinical applications. Its major mode of action is inhibition of the production of cytokines involved in the regulation of T-cell activation. In particular, cyclosporine inhibits the transcription of interleukin 2. Although cyclosporine's major actions are on T cells, there is some evidence that it produces direct effects on other cell types. Its immunosuppressive action is closely linked to its binding of cyclophilin, a member of a family of high-affinity

15 cyclosporine-binding proteins widely distributed in different cell types and in different species. The cyclophilins have been shown to have peptidyl-prolyl cis-trans isomerase enzyme activity that is blocked by cyclosporine. Although this may be a factor in cyclosporine's selective inhibition of cytokine gene transcription, it is still unclear whether inhibition of this activity is the mechanism through which cyclosporine exerts its effects on target cells. The

20 ubiquitous presence of cyclophilins raises the question of why cyclosporine has major effects on T cells. Perhaps the critical proteins affected are transcriptional regulators restricted in their tissue distribution. The effects of cyclosporine on T cells and, directly or indirectly, on connective tissue cells, all of which can produce a range of cytokines, are of interest in relation to the tissue changes that occur in such inflammatory conditions as rheumatoid arthritis.

25 PMID: 1502562

Panel CNS_1 Summary: Ag3122 This panel confirms the expression of this gene at low levels in the brain in an independent group of individuals. Please see Panel 1.3D for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

NOV40

30 Expression of NOV40/CG57157-01 was assessed using the primer-probe set Ag3123, described in Table AHA. Results of the RTQ-PCR runs are shown in TablesAHB.

Table AHA. Probe Name Ag3123

IL-4			
EOL-1 dbcAMP	3.5	Dermal fibroblast CCD1070 TNF alpha	63.3
EOL-1 dbcAMP PMA/ionomycin	0.9	Dermal fibroblast CCD1070 IL-1 beta	15.9
Dendritic cells none	2.1	Dermal fibroblast IFN gamma	10.4
Dendritic cells LPS	1.0	Dermal fibroblast IL-4	8.4
Dendritic cells anti-CD40	0.0	IBD Colitis 2	1.7
Monocytes rest	0.0	IBD Crohn's	1.9
Monocytes LPS	1.3	Colon	7.1
Macrophages rest	4.6	Lung	17.6
Macrophages LPS	0.0	Thymus	61.6
HUVEC none	17.8	Kidney	30.4
HUVEC starved	100.0		

Panel 1.3D Summary: Ag3123 Results from one experiment with the CG57157-01 gene are not included. The amp plot indicates that there were experimental difficulties with this run (data not shown).

Panel 4D Summary: Ag3123 The CG57157-01 gene is expressed at low levels in T cells and is also expressed at significant levels in endothelium, epithelium and fibroblasts as well as in normal thymus and kidney. Furthermore, treatment of proinflammatory mediators reduces the level of this transcript in HUVEC cells as compared to in starved cells. The protein encoded for by this transcript may be important in the normal function of the cell types that express it. Regulation of the protein encoded for by this transcript could be important for maintaining or resuming normal homeostasis.

NOV41

Expression of NOV41/CG57159-01 was assessed using the primer-probe set Ag3320, described in Table AIA. Results of the RTQ-PCR runs are shown in Tables AIB and AIC.

Table AIA. Probe Name Ag3320

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ttggtgataaatgtccctgc-3'	20	161	380
Probe	TET-5'-ggggtgtgtcagggtggtgacttc-3'-TAMRA	24	199	381
Reverse	5'-ccagtgcattatggtgtgt-3'	20	223	382

Table AIB. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3320, Run 215775833	Tissue Name	Rel. Exp.(%) Ag3320, Run 215775833
Adipose	0.0	Renal ca. TK-10	0.0
Melanoma* Hs688(A).T	0.0	Bladder	0.0
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	0.0	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	0.0

Squamous cell carcinoma SCC-4	0.0	Colon ca.* (SW480 met) SW620	0.0
Testis Pool	>0.0	Colon ca. HT29	0.0
Prostate ca.* (bone met) PC-3	0.0	Colon ca. HCT-116	0.0
Prostate Pool	0.0	Colon ca. CaCo-2	0.0
Placenta	0.0	Colon cancer tissue	0.0
Uterus Pool	0.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	0.0	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	0.0	Colon Pool	0.0
Ovarian ca. OVCAR-5	0.0	Small Intestine Pool	0.0
Ovarian ca. IGROV-1	0.0	Stomach Pool	0.1
Ovarian ca. OVCAR-8	0.0	Bone Marrow Pool	0.0
Ovary	0.0	Fetal Heart	0.0
Breast ca. MCF-7	0.0	Heart Pool	0.3
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	0.2
Breast ca. BT 549	0.0	Fetal Skeletal Muscle	0.0
Breast ca. T47D	0.0	Skeletal Muscle Pool	0.0
Breast ca. MDA-N	0.0	Spleen Pool	0.0
Breast Pool	0.0	Thymus Pool	0.0
Trachea	0.0	CNS cancer (glio/astro) U87-MG	0.0
Lung	0.6	CNS cancer (glio/astro) U-118-MG	0.0
Fetal Lung	0.0	CNS cancer (neuro;met) SK-N-AS	0.0
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	0.0	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	0.1	CNS cancer (glio) SNB-19	0.0
Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	0.0
Lung ca. A549	0.0	Brain (Amygdala) Pool	0.0
Lung ca. NCI-H526	0.0	Brain (cerebellum)	0.0
Lung ca. NCI-H23	0.0	Brain (fetal)	0.0
Lung ca. NCI-H460	0.0	Brain (Hippocampus) Pool	0.0
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	0.0
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	0.0
Liver	0.0	Brain (Thalamus) Pool	0.0
Fetal Liver	0.0	Brain (whole)	0.0
Liver ca. HepG2	0.0	Spinal Cord Pool	0.0
Kidney Pool	1.6	Adrenal Gland	0.0
Fetal Kidney	0.0	Pituitary gland Pool	0.0
Renal ca. 786-0	0.0	Salivary Gland	0.0
Renal ca. A498	0.0	Thyroid (female)	0.1
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.0	Pancreas Pool	100.0

CNS_neurodegeneration_v1.0 Summary: Ag3320 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3320 Expression of the CG57159-01 gene is restricted to a sample derived from pancreatic tissue (CT = 27.6). Thus, expression of this gene could be used to distinguish pancreas from the other samples in the panel. In

addition, therapeutic modulation of the activity of this gene or its protein product may prove useful in the treatment of metabolically related diseases, such as obesity and diabetes.

Panel 4D Summary: Ag3320 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

5 NOV42

Expression of gene NOV42A/CG57226-01 and NOV42B/CG57226-02 was assessed using the primer-probe set Ag3142, described in Table AJA. Results of the RTQ-PCR runs are shown in Tables AJB, AJC and AJD. Please note that CG57226-02 represents a full-length physical clone of the CG57226-01 gene, validating the prediction of the gene sequence.

10 Table AJA. Probe Name Ag3142

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-caaaacaatgagtcctcagttt-3'	22	504	383
Probe	TET-5'- atctgcactgccatggccaaatg-3'-TAMRA	23	529	384
Reverse	5'-ctgccaaagatcacatgctt-3'	20	562	385

Table AJB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3142, Run 209055796	Tissue Name	Rel. Exp.(%) Ag3142, Run 209055796
AD 1 Hippo	14.4	Control (Path) 3 Temporal Ctx	3.4
AD 2 Hippo	25.0	Control (Path) 4 Temporal Ctx	71.7
AD 3 Hippo	10.8	AD 1 Occipital Ctx	27.9
AD 4 Hippo	19.8	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	82.9	AD 3 Occipital Ctx	13.1
AD 6 Hippo	58.2	AD 4 Occipital Ctx	29.5
Control 2 Hippo	30.1	AD 5 Occipital Ctx	15.0
Control 4 Hippo	12.2	AD 6 Occipital Ctx	31.0
Hippo Control (Path) 3	9.0	Ctx Control 1 Occipital	7.1
Ctx AD 1 Temporal	49.0	Ctx Control 2 Occipital	32.5
Ctx AD 2 Temporal	28.5	Ctx Control 3 Occipital	0.0
Ctx AD 3 Temporal	11.3	Ctx Control 4 Occipital	11.4
Ctx AD 4 Temporal	47.0	Control (Path) 1 Occipital Ctx	100.0
AD 5 Inf Temporal Ctx	89.5	Control (Path) 2 Occipital Ctx	26.1
AD 5	49.7	Control (Path) 3	1.8

SupTemporal Ctx		Occipital Ctx	
AD 6 Inf Temporal Ctx	54.3	Control (Path) 4 Occipital Ctx	36.3
AD 6 Sup Temporal Ctx	69.3	Control 1 Parietal Ctx	9.0
Control 1 Temporal Ctx	11.5	Control 2 Parietal Ctx	57.0
Control 2 Temporal Ctx	20.3	Control 3 Parietal Ctx	13.6
Control 3 Temporal Ctx	21.3	Control (Path) 1 Parietal Ctx	54.7
Control 4 Temporal Ctx	11.0	Control (Path) 2 Parietal Ctx	34.4
Control (Path) 1 Temporal Ctx	66.0	Control (Path) 3 Parietal Ctx	9.0
Control (Path) 2 Temporal Ctx	55.1	Control (Path) 4 Parietal Ctx	65.5

Table AJC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag3142, Run 167994809	Tissue Name	Rel. Exp.(%) Ag3142, Run 167994809
Liver adenocarcinoma	16.6	Kidney (fetal)	20.2
Pancreas	6.8	Renal ca. 786-0	6.6
Pancreatic ca. CAPAN 2	5.7	Renal ca. A498	8.7
Adrenal gland	3.6	Renal ca. RXF 393	5.7
Thyroid	2.7	Renal ca. ACHN	2.4
Salivary gland	9.0	Renal ca. UO-31	1.1
Pituitary gland	9.7	Renal ca. TK-10	18.3
Brain (fetal)	16.7	Liver	11.3
Brain (whole)	12.8	Liver (fetal)	8.3
Brain (amygdala)	12.2	Liver ca. (hepatoblast) HepG2	11.0
Brain (cerebellum)	27.0	Lung	2.3
Brain (hippocampus)	13.9	Lung (fetal)	10.4
Brain (substantia nigra)	16.5	LX-1 Lung ca. (small cell)	16.6
Brain (thalamus)	4.7	NCI-H69 Lung ca. (small cell)	14.3
Cerebral Cortex	5.1	SHP-77 Lung ca. (s.cell var.)	78.5
Spinal cord	3.3	Lung ca. (large cell) NCI-H460	2.5
glio/astro U87-MG	13.5	Lung ca. (non-sm. cell) A549	25.0
glio/astro U-118-MG	11.1	NCI-H23 Lung ca. (non-s.cell)	12.4
astrocytoma SW1783	8.8	HOP-62 Lung ca. (non-s.cell)	16.0
neuro*; met SK-N-AS	28.7	NCI-H522 Lung ca. (non-s.cl)	12.6
astrocytoma SF-539	10.1	SW 900 Lung ca. (squam.)	16.5
astrocytoma SNB-75	13.2	NCI-H596 Lung ca. (squam.)	48.6
glioma SNB-19	30.4	Mammary gland	2.1
glioma U251	36.6	Breast ca.* (pl.ef)	14.7

		MCF-7	
glioma SF-295	13.6	Breast ca.* (pl.ef) MDA-MB-231	14.1
Heart (fetal)	0.6	Breast ca.* (pl.ef) T47D	57.8
Heart	8.7	Breast ca. BT-549	4.9
Skeletal muscle (fetal)	2.5	Breast ca. MDA-N	7.5
Skeletal muscle	2.9	Ovary	1.3
Bone marrow	8.0	Ovarian ca. OVCAR-3	23.0
Thymus	20.6	Ovarian ca. OVCAR-4	4.2
Spleen	7.6	Ovarian ca. OVCAR-5	100.0
Lymph node	26.6	Ovarian ca. OVCAR-8	4.9
Colorectal	20.3	Ovarian ca. IGROV-1	3.0
Stomach	9.5	Ovarian ca.* (ascites) SK-OV-3	66.4
Small intestine	15.6	Uterus	7.3
Colon ca. SW480	11.4	Placenta	0.0
Colon ca.* SW620(SW480 met)	59.5	Prostate	4.0
Colon ca. HT29	18.3	Prostate ca.* (bone met)PC-3	12.2
Colon ca. HCT-116	14.8	Testis	3.1
Colon ca. CaCo-2	26.8	Melanoma Hs688(A).T	3.9
Colon ca. tissue(ODO3866)	6.9	Melanoma* (met) Hs688(B).T	9.4
Colon ca. HCC-2998	28.7	Melanoma UACC-62	3.2
Gastric ca.* (liver met) NCI-N87	25.2	Melanoma M14	2.9
Bladder	51.4	Melanoma LOX IMVI	0.0
Trachea	2.4	Melanoma* (met) SK-MEL-5	6.6
Kidney	11.4	Adipose	21.8

Table AJD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3142, Run 164527962	Tissue Name	Rel. Exp.(%) Ag3142, Run 164527962
Secondary Th1 act	30.8	HUVEC IL-1beta	11.5
Secondary Th2 act	30.1	HUVEC IFN gamma	12.8
Secondary Tr1 act	34.6	gamma HUVEC TNF alpha + IFN	14.1
Secondary Th1 rest	7.1	HUVEC TNF alpha + IL4	7.6
Secondary Th2 rest	20.4	HUVEC IL-11	7.7
Secondary Tr1 rest	21.0	none Lung Microvascular EC	14.9
Primary Th1 act	32.1	Lung Microvascular EC TNFalpha + IL-1beta	19.6
Primary Th2 act	46.3	none Microvascular Dermal EC	17.9
Primary Tr1 act	47.3	Microsvasular Dermal EC	11.3

Monocytes LPS	18.9	Colon	20.9
Macrophages rest	11.1	Lung	8.3
Macrophages LPS	11.7	Thymus	29.3
HUVEC none	10.0	Kidney	51.1
HUVEC starved	23.3		

CNS_neurodegeneration_v1.0 Summary: Ag3142 This panel confirms the expression of this gene at moderate to low levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.3D for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

Panel 1.3D Summary: Ag3142 The CG57226-01 gene is expressed at low to moderate levels in the majority of samples on this panel, with highest expression in ascites derived ovarian cancer cell line OVCAR-5 (CT=30.4). It is also expressed in melanoma, prostate, breast, lung, renal, gastric, colon, neuroblastoma, pancreatic and liver adenocarcinoma cell lines. Hence, this gene is likely to play a role in cell survival and proliferation.

Among tissues with metabolic or endocrine function, this gene is expressed in pituitary gland, liver, adipose, and pancreas. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

This gene is expressed at low levels throughout the CNS, including in amygdala, hippocampus, substantia nigra, thalamus, cerebellum, and cerebral cortex. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

Panel 4D Summary: Ag3142 The CG57226-01 gene is expressed at moderate levels in a wide range of cell types of significance in the immune response in health and disease. These cells include members of the T-cell, B-cell, endothelial cell, macrophage/monocyte/dendritic cell, basophil, eosinophil and peripheral blood mononuclear cell family, as well as epithelial and fibroblast cell types from lung and skin, and normal tissues represented by colon, lung, thymus and kidney. This ubiquitous pattern of expression suggests that this gene product may be involved in homeostatic processes for these and other cell types and tissues.

This pattern is in agreement with the expression profile in Panel 1.3D and also suggests a role for the gene product in cell survival and proliferation.

Therefore, therapeutic modulation of the activity of this gene or its protein product may lead to the alteration of functions associated with these cell types and lead to improvement of the symptoms of patients suffering from autoimmune and inflammatory diseases such as asthma, allergies, inflammatory bowel disease, lupus erythematosus, psoriasis, rheumatoid arthritis, and osteoarthritis.

NOV43

Expression of NOV43/CG57538-01 was assessed using the primer-probe set Ag3277, described in Table AKA. Results of the RTQ-PCR runs are shown in Table AKB.

Table AKA. Probe Name Ag3277

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-caaccctggtcaaataattcaa-3'	22	2424	386
Probe	TET-5'-aaaataaagccgcaagaccgtattct-3'-TAMRA	26	2456	387
Reverse	5'-ttttcactccatgagcatgaat-3'	22	2482	388

Table AKB. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3277, Run 164635110	Tissue Name	Rel. Exp.(%) Ag3277, Run 164635110
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	2.6
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	8.7
Secondary Th1 rest	2.8	HUVEC TNF alpha + IL4	2.3
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	4.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	4.5
Primary Th2 act	0.0	Microvascular Dermal EC none	6.4
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	6.7	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	7.6
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	5.1	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	44.8
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0

LAK cells IL-2	0.0	Liver cirrhosis	6.1
LAK cells IL-2+IL-12	0.0	Lupus kidney	4.1
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	14.5
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	100.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	27.4
NK Cells IL-2 rest	17.4	NCI-H292 IL-13	37.4
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	8.2
Two Way MLR 5 day	4.7	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	3.9	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	9.5
EOL-1 dbcAMP PMA/ionomycin	12.2	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	2.3	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	5.2	Colon	0.0
Macrophages rest	0.0	Lung	3.2
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	4.2	Kidney	15.1
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag3277 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3277 Results from one experiment with the CG57538-01 gene are not included. The amp plot indicates that there were experimental difficulties with this run (data not shown).

Panel 4D Summary: Ag3277 Highest expression of the CG57538-01 gene, a Ceruloplasmin homolog, is in samples derived from the pulmonary mucoepidermoid cell line NCI-H292 stimulated with IL-4 (CTs=34.4). Thus, this expression profile indicates that this gene product may play a key role as a mediator of inflammation, especially in late-phase allergic reactions, and as a mediator of local cellular movement or trafficking into the inflamed area by cytokines and chemokines. Airway epithelial cells are believed to be the major source of Ceruloplasmin in the lung fluid and may play critical role in host defense against oxidative damage and infection in the lung (ref. 1).

References:

1. Yang F, Friedrichs WE, deGraffenried L, Herbert DC, Weaker FJ, Bowman BH, Coalson JJ. Cellular expression of ceruloplasmin in baboon and mouse lung during development and inflammation. Am J Respir Cell Mol Biol 1996 Feb;14(2):161-9

Abstract - Ceruloplasmin (CP) is an important extracellular antioxidant and free radical scavenger. Although CP is expressed mainly in the liver, recent studies have identified the lung as another major site of CP synthesis. The sites and cell types that are responsible for CP expression in baboon and mouse lung are described. CP mRNA is detected in primordial bronchial epithelium in baboon fetuses by 60 days of gestation. At 140 days of gestation and thereafter, CP mRNA is found in airway epithelium and in the ductal cells of the submucosal glands. In developing and mature mice, CP mRNA is present in epithelial cells throughout the airway. In endotoxin-treated mice, the amount of CP mRNA increases several-fold in large airways but increases only moderately in small airways. This suggests that the high concentration of CP in the mucus lining of the upper airway, which serves to filter harmful substances, is particularly important during stressful conditions. Endotoxin treatment in mice also results in the induction of high levels of CP mRNA in a subset of alveolar wall cells. The data suggest that the airway epithelial cells are the major source of CP in the lung fluid and support ceruloplasmin's critical role in host defense against oxidative damage and infection in the lung.

NOV44

Expression of NOV44A/CG57623-01 and NOV44B/CG57623-02 was assessed using the primer-probe set Ag3296, described in Table AKA. Results of the RTQ-PCR runs are shown in Tables AKB, AKC and AKD. Please note that CG57623-02 represents a full-length physical clone of the CG57623-01 gene, validating the prediction of the gene sequence.

Table ALA. Probe Name Ag3296

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-agaccatctttccaatctgat-3'	22	737	389
Probe	TET-5'-caattccatggccaaggactcctg-3'-TAMRA	24	765	390
Reverse	5'-gttccaagtcacctccagtctt-3'	22	791	391

Table ALB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3296, Run 210063000	Tissue Name	Rel. Exp.(%) Ag3296, Run 210063000
AD 1 Hippo	19.5	Control (Path) 3 Temporal	9.8

		Ctx	
AD 2 Hippo	3.0	Control (Path) 4 Temporal Ctx	4.3
AD 3 Hippo	6.5	AD 1 Occipital Ctx	10.9
AD 4 Hippo	39.5	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	26.6	AD 3 Occipital Ctx	10.4
AD 6 Hippo	84.7	AD 4 Occipital Ctx	6.5
Control 2 Hippo	10.8	AD 5 Occipital Ctx	5.1
Control 4 Hippo	33.7	AD 6 Occipital Ctx	0.0
Control (Path) 3 Hippo	16.4	Control 1 Occipital Ctx	12.6
AD 1 Temporal Ctx	18.3	Control 2 Occipital Ctx	7.4
AD 2 Temporal Ctx	4.7	Control 3 Occipital Ctx	0.0
AD 3 Temporal Ctx	4.3	Control 4 Occipital Ctx	4.2
AD 4 Temporal Ctx	15.8	Control (Path) 1 Occipital Ctx	12.5
AD 5 Inf Temporal Ctx	100.0	Control (Path) 2 Occipital Ctx	0.0
AD 5 Sup Temporal Ctx	83.5	Control (Path) 3 Occipital Ctx	2.3
AD 6 Inf Temporal Ctx	39.0	Control (Path) 4 Occipital Ctx	0.0
AD 6 Sup Temporal Ctx	18.0	Control 1 Parietal Ctx	12.6
Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	13.2
Control 2 Temporal Ctx	13.5	Control 3 Parietal Ctx	9.7
Control 3 Temporal Ctx	4.7	Control (Path) 1 Parietal Ctx	24.5
Control 3 Temporal Ctx	15.8	Control (Path) 2 Parietal Ctx	0.0
Control (Path) 1 Temporal Ctx	16.3	Control (Path) 3 Parietal Ctx	0.0
Control (Path) 2 Temporal Ctx	10.3	Control (Path) 4 Parietal Ctx	3.3

Table ALC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3296, Run 215669667	Tissue Name	Rel. Exp.(%) Ag3296, Run 215669667
Adipose	6.3	Renal ca. TK-10	0.0
Melanoma* Hs688(A).T	0.0	Bladder	25.7
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMV1	0.0	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	1.2	Colon ca. SW480	0.0
Squamous cell carcinoma SCC-4	0.0	Colon ca.* (SW480 met) SW620	0.0
Testis Pool	47.6	Colon ca. HT29	0.0
Prostate ca.* (bone met) PC-3	0.0	Colon ca. HCT-116	0.0
Prostate Pool	4.1	Colon ca. CaCo-2	0.0
Placenta	1.1	Colon cancer tissue	12.9
Uterus Pool	3.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	1.8	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	1.0	Colon Pool	19.5
Ovarian ca. OVCAR-5	6.8	Small Intestine Pool	10.4

Ovarian ca. IGROV-1	0.0	Stomach Pool	6.3
Ovarian ca. OVCAR-8	0.0	Bone Marrow Pool	4.3
Ovary	18.9	Fetal Heart	5.7
Breast ca. MCF-7	0.0	Heart Pool	5.3
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	14.6
Breast ca. BT 549	0.0	Fetal Skeletal Muscle	12.2
Breast ca. T47D	5.6	Skeletal Muscle Pool	3.3
Breast ca. MDA-N	0.0	Spleen Pool	87.1
Breast Pool	25.7	Thymus Pool	25.3
Trachea	26.2	CNS cancer (glio/astro) U87-MG	0.9
Lung	2.2	CNS cancer (glio/astro) U-118-MG	7.5
Fetal Lung	100.0	CNS cancer (neuro;met) SK-N-AS	0.0
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	0.0	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	0.0	CNS cancer (glio) SNB-19	0.0
Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	0.0
Lung ca. A549	0.0	Brain (Amygdala) Pool	11.3
Lung ca. NCI-H526	0.0	Brain (cerebellum)	1.3
Lung ca. NCI-H23	22.4	Brain (fetal)	1.2
Lung ca. NCI-H460	5.7	Brain (Hippocampus) Pool	10.7
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	2.4
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	4.4
Liver	2.4	Brain (Thalamus) Pool	7.1
Fetal Liver	8.4	Brain (whole)	3.4
Liver ca. HepG2	0.0	Spinal Cord Pool	11.0
Kidney Pool	13.8	Adrenal Gland	8.4
Fetal Kidney	17.8	Pituitary gland Pool	3.4
Renal ca. 786-0	0.0	Salivary Gland	3.3
Renal ca. A498	0.0	Thyroid (female)	1.5
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.0	Pancreas Pool	16.8

Table ALD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3296, Run 164633942	Tissue Name	Rel. Exp.(%) Ag3296, Run 164633942
Secondary Th1 act	0.2	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.2	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.6	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.6	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.5	Small airway epithelium none	0.0
Primary Tr1 rest	0.5	Small airway epithelium TNFalpha + IL-1beta	0.3
CD45RA CD4 lymphocyte	3.1	Coronary artery SMC rest	0.0

act			
CD45RO CD4 lymphocyte act	2.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.6	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	1.9	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	18.7	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.9	Liver cirrhosis	1.4
LAK cells IL-2+IL-12	5.5	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	4.6	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	4.8	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	21.2	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	2.7	NCI-H292 IL-13	0.0
Two Way MLR 3 day	12.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	3.7	HPAEC none	0.0
Two Way MLR 7 day	0.8	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	8.1	Lung fibroblast none	0.0
PBMC PWM	12.6	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	14.9	Lung fibroblast IL-4	0.3
Ramos (B cell) none	21.2	Lung fibroblast IL-9	0.2
Ramos (B cell) ionomycin	83.5	Lung fibroblast IL-13	0.3
B lymphocytes PWM	39.5	Lung fibroblast IFN gamma	0.3
B lymphocytes CD40L and IL-4	100.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	18.4	Dermal fibroblast CCD1070 TNF alpha	0.4
EOL-1 dbcAMP PMA/ionomycin	55.5	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	21.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	10.3	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	35.8	IBD Colitis 2	1.6
Monocytes rest	25.9	IBD Crohn's	0.0
Monocytes LPS	11.3	Colon	4.6
Macrophages rest	27.5	Lung	4.5
Macrophages LPS	13.7	Thymus	2.2
HUVEC none	0.0	Kidney	15.3
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag3296 This panel confirms the expression of this gene at low levels in the brains of an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3296 Expression of this gene is primarily associated with normal tissues rather than cancer cell lines. Expression of the CG57623-01 gene is highest in the fetal lung (CT = 31.1). Interestingly, this gene is expressed at higher levels in fetal lung (CT = 31.1) when compared to adult lung (CT = 36.6), suggesting that expression of this gene can be used to distinguish fetal from adult lung.

This gene is also expressed at low levels in several regions of the brain, including amygdala, hippocampus, thalamus and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

Among tissues with metabolic or endocrine function, this gene is expressed at low levels in adrenal gland, pancreas, fetal skeletal muscle, and fetal liver. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

Panel 4D Summary: Ag3296 The CG57623-01 gene is expressed at highest levels in activated B lymphocytes, represented by ionomycin-activated Ramos and CD40L and IL-4 or pokeweed mitogen-activated B lymphocytes. Therefore, small molecule drugs or antibodies that antagonize the function of this gene product may be useful as therapeutic drugs to reduce or eliminate the symptoms in patients with autoimmune and inflammatory diseases in which B cells play a part in the initiation or progression of the disease process, such as lupus erythematosus, Crohn's disease, ulcerative colitis, multiple sclerosis, chronic obstructive pulmonary disease, asthma, emphysema, rheumatoid arthritis, or psoriasis.

NOV45

Expression of NOV45A/CG57656-01 and NOV45B/CG57656-02 was assessed using the primer-probe sets Ag3298 and Ag4482, described in Tables AMA and AMB. Results of the RTQ-PCR runs are shown in Tables AMC, AMD, AME and AMF. Please note that primer-probe set Ag4482 is specific for CG57656-02.

Table AMA. Probe Name Ag3298

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-cagacctatgcaacctctggtta-3'	22	3390	392
Probe	TET-5'-agctgcgacatacaagccaaggcat-3'-TAMRA	25	3422	393
Reverse	5'-ggtaaggcagcacaggtatg-3'	20	3450	394

Table AMB. Probe Name Ag4482

Primers	Sequences	Length	Start Position	SEQ ID NO
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Forward	5'-gaggtggtcactgtgatcactt-3'	22	1804	395
Probe	TET-5'-ttacaactccagaaccctggtgctg-3'-TAMRA	26	1838	396
Reverse	5'-ctgagtcgattggctatgag-3'	21	1882	397

Table AMC. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3298, Run 210063510	Rel. Exp.(%) Ag4482, Run 224535697	Tissue Name	Rel. Exp.(%) Ag3298, Run 210063510	Rel. Exp.(%) Ag4482, Run 224535697
AD 1 Hippo	6.0	6.9	Control (Path) 3 Temporal Ctx	20.3	3.9
AD 2 Hippo	25.5	24.7	Control (Path) 4 Temporal Ctx	54.3	43.2
AD 3 Hippo	9.5	6.2	AD 1 Occipital Ctx	48.0	12.9
AD 4 Hippo	16.0	8.4	AD 2 Occipital Ctx (Missing)	0.0	0.0
AD 5 Hippo	100.0	100.0	AD 3 Occipital Ctx	17.6	6.6
AD 6 Hippo	34.6	27.7	AD 4 Occipital Ctx	38.7	20.2
Control 2 Hippo	19.9	12.3	AD 5 Occipital Ctx	30.1	42.6
Control 4 Hippo	23.2	10.0	AD 6 Occipital Ctx	47.6	23.7
Control (Path) 3 Hippo	12.9	5.5	Control 1 Occipital Ctx	10.0	3.1
AD 1 Temporal Ctx	42.3	12.3	Control 2 Occipital Ctx	43.2	38.7
AD 2 Temporal Ctx	35.4	34.6	Control 3 Occipital Ctx	66.4	22.2
AD 3 Temporal Ctx	24.3	9.1	Control 4 Occipital Ctx	20.7	4.8
AD 4 Temporal Ctx	61.6	24.3	Control (Path) 1 Occipital Ctx	76.3	96.6
AD 5 Inf Temporal Ctx	79.0	59.9	Control (Path) 2 Occipital Ctx	38.7	17.1
AD 5 Sup Temporal Ctx	45.1	39.0	Control (Path) 3 Occipital Ctx	4.9	1.4
AD 6 Inf Temporal Ctx	65.1	42.6	Control (Path) 4 Occipital Ctx	67.8	32.1
AD 6 Sup Temporal Ctx	64.6	57.4	Control 1 Parietal Ctx	27.9	7.8
Control 1 Temporal Ctx	25.9	6.7	Control 2 Parietal Ctx	70.2	49.3
Control 2 Temporal Ctx	30.1	22.1	Control 3 Parietal Ctx	34.6	18.4
Control 3 Temporal Ctx	56.6	19.5	Control (Path) 1 Parietal Ctx	61.1	68.8
Control 3 Temporal Ctx	31.6	13.6	Control (Path) 2 Parietal Ctx	46.7	33.0
Control (Path) 1 Temporal Ctx	71.2	76.8	Control (Path) 3 Parietal Ctx	7.6	3.4
Control (Path) 2 Temporal Ctx	76.3	50.0	Control (Path) 4 Parietal Ctx	78.5	54.7

Table AMD. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3298, Run 215601953	Rel. Exp.(%) Ag3298, Run 216607677	Rel. Exp.(%) Ag3298, Run 222691295	Rel. Exp.(%) Ag4482, Run 222666310
Adipose	0.2	0.9	1.9	0.7

Melanoma* Hs688(A).T	0.0	0.0	0.0	0.0
Melanoma* Hs688(B).T	0.1	0.2	0.0	0.1
Melanoma* M14	0.0	0.0	0.0	0.0
Melanoma* LOXIMVI	2.1	2.5	3.3	1.7
Melanoma* SK-MEL-5	2.4	2.2	1.5	3.7
Squamous cell carcinoma SCC-4	0.1	0.2	0.1	0.1
Testis Pool	5.5	7.3	7.9	5.6
Prostate ca.* (bone met) PC-3	0.9	1.4	0.5	1.1
Prostate Pool	5.5	4.5	4.5	2.4
Placenta	0.5	0.7	0.7	0.6
Uterus Pool	2.5	1.5	1.6	2.7
Ovarian ca. OVCAR-3	0.0	0.1	0.0	0.0
Ovarian ca. SK-OV-3	0.0	0.0	0.0	0.0
Ovarian ca. OVCAR-4	0.1	0.0	0.0	0.1
Ovarian ca. OVCAR-5	20.2	19.1	21.6	13.7
Ovarian ca. IGROV-1	0.0	0.4	0.4	0.1
Ovarian ca. OVCAR-8	0.0	0.0	0.0	0.0
Ovary	0.5	0.7	0.3	0.6
Breast ca. MCF-7	3.0	2.1	2.1	1.6
Breast ca. MDA-MB-231	0.0	0.0	0.0	0.0
Breast ca. BT 549	0.6	0.2	0.5	0.2
Breast ca. T47D	45.4	52.5	43.5	17.0
Breast ca. MDA-N	0.0	0.0	0.0	0.0
Breast Pool	10.4	10.8	12.5	9.0
Trachea	1.4	4.9	4.6	2.5
Lung	0.8	1.0	0.7	0.5
Fetal Lung	6.5	7.0	5.7	5.2
Lung ca. NCI-N417	16.3	14.8	13.6	4.0
Lung ca. LX-1	12.9	15.7	11.4	13.1
Lung ca. NCI-H146	4.3	5.6	5.2	2.2
Lung ca. SHP-77	7.4	5.2	5.0	7.9
Lung ca. A549	2.2	1.1	1.1	1.1
Lung ca. NCI-H526	25.5	21.6	18.7	6.8
Lung ca. NCI-H23	9.2	4.9	4.1	3.8
Lung ca. NCI-H460	1.4	0.4	1.0	0.5
Lung ca. HOP-62	0.2	0.0	0.2	0.1
Lung ca. NCI-H522	3.5	2.2	4.2	3.2
Liver	0.0	0.0	0.0	0.0
Fetal Liver	0.1	0.4	0.1	0.1
Liver ca. HepG2	0.0	0.0	0.0	0.0
Kidney Pool	51.8	62.0	59.0	27.0
Fetal Kidney	3.1	3.9	2.6	1.4
Renal ca. 786-0	0.0	0.0	0.0	0.0
Renal ca. A498	0.1	0.1	0.2	0.0
Renal ca. ACHN	0.0	0.1	0.2	0.2
Renal ca. UO-31	2.6	1.2	2.0	0.9
Renal ca. TK-10	1.5	1.9	1.7	2.3
Bladder	2.2	1.5	1.7	1.2
Gastric ca. (liver met.) NCI-N87	100.0	93.3	94.0	100.0
Gastric ca. KATO III	97.3	85.3	100.0	62.4

Colon ca. SW-948	8.1	6.9	7.7	2.0
Colon ca. SW480	32.5	37.6	16.4	23.7
Colon ca. * (SW480 met) SW620	4.3	6.6	3.9	4.6
Colon ca. HT29	2.5	3.3	3.8	2.8
Colon ca. HCT-116	9.3	11.7	12.7	8.7
Colon ca. CaCo-2	2.2	1.9	2.9	2.1
Colon cancer tissue	0.4	0.9	0.8	0.3
Colon ca. SW1116	13.7	15.2	11.9	4.2
Colon ca. Colo-205	15.4	8.9	12.4	2.8
Colon ca. SW-48	0.0	0.0	0.0	0.1
Colon Pool	13.4	17.9	16.8	11.0
Small Intestine Pool	19.3	19.2	19.8	12.0
Stomach Pool	6.6	7.2	7.9	4.5
Bone Marrow Pool	2.4	4.3	6.6	5.5
Fetal Heart	9.0	12.3	16.5	9.4
Heart Pool	6.2	8.6	8.0	5.3
Lymph Node Pool	22.1	18.2	25.5	15.8
Fetal Skeletal Muscle	2.4	2.6	1.9	1.2
Skeletal Muscle Pool	1.6	2.4	1.1	1.2
Spleen Pool	1.7	3.0	2.4	2.0
Thymus Pool	4.1	5.0	8.0	2.4
CNS cancer (glio/astro) U87-MG	5.1	4.7	4.6	2.8
CNS cancer (glio/astro) U-118-MG	78.5	100.0	80.7	69.7
CNS cancer (neuro;met) SK-N-AS	5.1	5.3	6.2	4.9
CNS cancer (astro) SF-539	0.0	0.0	0.0	0.0
CNS cancer (astro) SNB-75	7.1	9.5	10.4	5.6
CNS cancer (glio) SNB-19	0.2	0.0	0.2	0.1
CNS cancer (glio) SF-295	5.6	4.7	4.2	4.1
Brain (Amygdala) Pool	5.9	7.3	5.8	2.4
Brain (cerebellum)	59.5	56.3	55.5	37.9
Brain (fetal)	10.7	12.0	15.1	8.7
Brain (Hippocampus) Pool	5.6	5.1	5.8	3.4
Cerebral Cortex Pool	7.5	7.9	7.3	4.4
Brain (Substantia nigra) Pool	9.9	8.8	9.5	3.8
Brain (Thalamus) Pool	11.3	8.8	9.6	5.8
Brain (whole)	11.6	12.8	17.1	8.5
Spinal Cord Pool	2.0	2.6	5.3	2.0
Adrenal Gland	1.6	2.7	2.0	1.4
Pituitary gland Pool	2.5	2.8	2.4	1.4
Salivary Gland	0.2	0.3	0.5	0.3
Thyroid (female)	3.5	5.0	4.8	2.3
Pancreatic ca. CAPAN2	8.2	4.9	6.4	6.8
Pancreas Pool	12.5	12.8	9.1	7.9

Table AME. Panel 4.1D

Tissue Name	Rel. Exp.(%) Ag4482, Run 195476203	Tissue Name	Rel. Exp.(%) Ag4482, Run 195476203
Secondary Th1 act	18.7	HUVEC IL-1beta	2.1
Secondary Th2 act	24.0	HUVEC IFN gamma	2.0
Secondary Tr1 act	15.1	HUVEC TNF alpha + IFN gamma	1.5
Secondary Th1 rest	40.6	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	43.2	HUVEC IL-11	0.0
Secondary Tr1 rest	90.8	Lung Microvascular EC none	0.0
Primary Th1 act	54.7	Lung Microvascular EC TNFalpha + IL-1beta	0.5
Primary Th2 act	92.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	75.3	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	60.3	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	49.0	Small airway epithelium none	0.0
Primary Tr1 rest	84.7	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	26.2	Coronary artery SMC rest	0.3
CD45RO CD4 lymphocyte act	42.0	Coronary artery SMC TNFalpha + IL-1beta	0.5
CD8 lymphocyte act	33.9	Astrocytes rest	16.4
Secondary CD8 lymphocyte rest	60.7	Astrocytes TNFalpha + IL-1beta	15.3
Secondary CD8 lymphocyte act	13.9	KU-812 (Basophil) rest	52.9
CD4 lymphocyte none	41.8	KU-812 (Basophil) PMA/ionomycin	92.7
2ry Th1/Th2/Tr1_anti-CD95 CH11	68.8	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	40.3	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	26.1	Liver cirrhosis	1.7
LAK cells IL-2+IL-12	32.8	NCI-H292 none	0.0
LAK cells IL-2+IFN gamma	34.4	NCI-H292 IL-4	0.0
LAK cells IL-2+ IL-18	50.3	NCI-H292 IL-9	1.3
LAK cells PMA/ionomycin	100.0	NCI-H292 IL-13	0.7
NK Cells IL-2 rest	29.7	NCI-H292 IFN gamma	0.0
Two Way MLR 3 day	28.7	HPAEC none	0.6
Two Way MLR 5 day	21.8	HPAEC TNF alpha + IL-1 beta	0.7
Two Way MLR 7 day	20.7	Lung fibroblast none	0.0
PBMC rest	14.1	Lung fibroblast TNF alpha + IL-1 beta	0.6
PBMC PWM	32.8	Lung fibroblast IL-4	1.3
PBMC PHA-L	88.3	Lung fibroblast IL-9	1.0
Ramos (B cell) none	0.0	Lung fibroblast IL-13	0.6
Ramos (B cell) ionomycin	0.0	Lung fibroblast IFN gamma	1.6
B lymphocytes PWM	23.8	Dermal fibroblast CCD1070 rest	2.7
B lymphocytes CD40L and IL-4	9.7	Dermal fibroblast CCD1070 TNF alpha	32.3
EOL-1 dbcAMP	0.6	Dermal fibroblast CCD1070 IL-1 beta	1.4
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast IFN gamma	1.4
Dendritic cells none	5.0	Dermal fibroblast IL-4	1.2

Dendritic cells LPS	0.8	Dermal Fibroblasts rest	2.2
Dendritic cells anti-CD40	0.0	Neutrophils TNFa+LPS	0.8
Monocytes rest	0.6	Neutrophils rest	0.6
Monocytes LPS	0.0	Colon	19.3
Macrophages rest	0.8	Lung	3.1
Macrophages LPS	0.0	Thymus	18.9
HUVEC none	0.0	Kidney	7.5
HUVEC starved	0.0		

Table AMF, Panel 4D

Tissue Name	Rel. Exp.(%) Ag3298, Run 164682520	Tissue Name	Rel. Exp.(%) Ag3298, Run 164682520
Secondary Th1 act	18.9	HUVEC IL-1beta	0.0
Secondary Th2 act	20.4	HUVEC IFN gamma	0.9
Secondary Tr1 act	19.6	HUVEC TNF alpha + IFN gamma	2.5
Secondary Th1 rest	40.3	HUVEC TNF alpha + IL4	1.1
Secondary Th2 rest	34.4	HUVEC IL-11	0.0
Secondary Tr1 rest	100.0	Lung Microvascular EC none	0.0
Primary Th1 act	38.2	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	56.3	Microvascular Dermal EC none	0.0
Primary Tr1 act	49.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	87.1	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	63.7	Small airway epithelium none	0.0
Primary Tr1 rest	58.6	Small airway epithelium TNFalpha + IL-1beta	0.1
CD45RA CD4 lymphocyte act	27.2	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	31.9	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	46.0	Astrocytes rest	58.2
Secondary CD8 lymphocyte rest	41.8	Astrocytes TNFalpha + IL-1beta	13.2
Secondary CD8 lymphocyte act	10.4	KU-812 (Basophil) rest	24.8
CD4 lymphocyte none	26.1	KU-812 (Basophil) PMA/ionomycin	52.9
2ry Th1/Th2/Tr1_anti-CD95 CH11	31.9	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	24.3	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	11.7	Liver cirrhosis	10.6
LAK cells IL-2+IL-12	29.3	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	35.8	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	32.3	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	59.5	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	21.8	NCI-H292 IL-13	0.0
Two Way MLR 3 day	22.4	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	17.2	HPAEC none	0.0
Two Way MLR 7 day	17.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	15.1	Lung fibroblast none	0.0
PBMC PWM	37.9	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	51.4	Lung fibroblast IL-4	0.0

Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	12.4	Lung fibroblast IFN gamma	2.4
B lymphocytes CD40L and IL-4	10.2	Dermal fibroblast CCD1070 rest	0.5
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	12.8
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	1.9	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	1.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	3.0
Monocytes rest	0.7	IBD Crohn's	0.0
Monocytes LPS	0.4	Colon	54.7
Macrophages rest	0.9	Lung	13.8
Macrophages LPS	1.4	Thymus	7.8
HUVEC none	1.0	Kidney	14.8
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag3298/Ag4482 Results from two experiments using different probe/primer sets are in excellent agreement. This panel confirms the expression of this gene at moderate levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between
5 Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3298/Ag4482 Results from four experiments using two different probe/primer sets are in excellent agreement, with highest
10 expression of the CG57656-02 gene in two samples derived from gastric cancer cell lines (CTs=27.5). Interestingly, expression of this gene is much higher in the gastric cancer cell lines than in normal stomach. Thus, expression of this gene could be used to differentiate between these samples and other samples on this panel and as a marker for gastric cancer. Furthermore, therapeutic modulation of the activity of this gene or its protein product, using
15 small molecule drugs, antibodies or protein therapeutics, could be of benefit in the treatment of gastric cancer.

This gene is also expressed at moderate levels throughout the CNS, including in amygdala, hippocampus, substantia nigra, thalamus, cerebral cortex, and spinal cord, and at high levels in the cerebellum. Therefore, this gene may play a role in central nervous system
20 disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

The CG57656-02 gene encodes a protein with similarity to the *Drosophila* turtle protein, a member of the Ig superfamily (IgSF). In *Drosophila*, the turtle (tutl) protein is expressed in the CNS and in a small, defined subset of the peripheral nervous system (PNS). Alternative splicing of the primary transcript results in membrane-bound and secreted Tutl isoforms that are essential for development and adult viability. In addition, tutl function is required for establishing a nervous system capable of executing complex forms of coordinated movement such as tactile escape response, coordinated righting behavior in larval and adult stages, and flight in adulthood (ref. 1).

Among tissues with metabolic or endocrine function, this gene is expressed at moderate levels in pancreas and heart and at low levels in thyroid, pituitary gland, adrenal gland, and skeletal muscle. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

References:

1. Bodily KD, Morrison CM, Renden RB, Broadie K. A novel member of the Ig superfamily, turtle, is a CNS specific protein required for coordinated motor control. *J Neurosci* 2001 May 1;21(9):3113-25

We describe here the cloning and functional characterization of a neural-specific novel member of the Ig superfamily, turtle (tutl), with a structure of five Ig C2-type domains, two fibronectin type III domains, and one transmembrane region. Alternative splicing of the tutl gene produces at least four Tutl isoforms, including two transmembrane proteins and two secreted proteins, with primary structures closely related to a human brain protein (KIAA1355), the Deleted in Colorectal Cancer/Neogenin/Frazzled receptor family, and the Roundabout/Dutt1 receptor family. An allelic series of tutl gene mutations resulted in recessive lethality to semilethality, indicating that the gene is essential. In contrast to other family members, tutl does not play a detectable role in axon pathfinding or nervous system morphogenesis. Likewise, basal synaptic transmission and locomotory movement are unaffected. However, tutl mutations cause striking movement defects exhibited in specific types of highly coordinated behavior. Specifically, tutl mutants display an abnormal response to tactile stimulation, the inability to regain an upright position from an inverted position (hence, "turtle"), and the inability to fly in adulthood. These phenotypes demonstrate that tutl plays an essential role in establishing a nervous system capable of executing coordinated motor output in complex behaviors.

PMID: 11312296

Panel 4.1D Summary: Ag4482 The CG57656-02 gene is expressed at highest levels in stimulated lymphokine-activated killer cells (LAK). LAK cells are involved in tumor immunology and cell clearance of virally and bacterial infected cells as well as tumors.

5 In addition, expression of this gene is upregulated in resting dermal fibroblast CCD1070 (CT = 35.7) by treatment with TNF alpha (CT = 32.1). Expression of this gene in stimulated dermal fibroblasts suggests that this gene may be important in the treatment of psoriasis.

10 The CG57656-02 gene encodes a protein with similarity to the Drosophila turtle protein, a member of the Ig superfamily (IgSF). The 5 Ig domains and 2 fibronectin domains in this membrane protein are characteristic of several types of cell surface receptors and cell adhesion molecules.

15 In addition to the utility in treatment of psoriasis, the expression of this gene in basophils and several types of T lymphocyte preparations suggests that antibodies or small molecules that antagonize the function of the CG57656-02 protein may be useful in reduction or elimination of the symptoms of various T cell-dependent or basophil-dependent medical conditions, such as, but not limited to, Crohn's disease, ulcerative colitis, multiple sclerosis, chronic obstructive pulmonary disease, asthma, emphysema, rheumatoid arthritis, and lupus erythematosus.

20 Furthermore, the extracellular domain of this protein may function to block the binding of the cognate ligand of the CG57656-02 protein on neighboring cells. This may modulate the function of T lymphocytes and basophils, and be useful as a protein therapeutic to reduce or eliminate the symptoms in the symptoms of various T cell-dependent or basophil-dependent medical conditions, such as, but not limited to, Crohn's disease, ulcerative colitis, multiple
25 sclerosis, chronic obstructive pulmonary disease, asthma, emphysema, rheumatoid arthritis, and lupus erythematosus, or psoriasis.

Panel 4D Summary: Ag3298 Results using this probe/primer set are in excellent agreement with those obtained using Ag4482 on Panel 4.1D. Please see Panel 4.1D for a description of the potential utility of this gene in immune function.

30 **NOV46**

Expression of NOV46/CG57682-01 was assessed using the primer-probe set Ag3308, described in Table ANA. Results of the RTQ-PCR runs are shown in Tables ANB, ANC and AND.

Table ANA. Probe Name Ag3308

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gcaacaaattcctgaagatcag-3'	22	1153	398
Probe	TET-5'-cctcagctgaactcaaaagccatcaa-3'-TAMRA	26	1182	399
Reverse	5'-atcagaggggaaggcaaggt-3'	19	1210	400

5 Table ANB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3308, Run 210143040	Tissue Name	Rel. Exp.(%) Ag3308, Run 210143040
AD 1 Hippo	5.0	Control (Path) 3 Temporal Ctx	9.9
AD 2 Hippo	25.2	Control (Path) 4 Temporal Ctx	36.6
AD 3 Hippo	14.6	AD 1 Occipital Ctx	46.3
AD 4 Hippo	4.4	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	100.0	AD 3 Occipital Ctx	17.2
AD 6 Hippo	37.1	AD 4 Occipital Ctx	33.9
Control 2 Hippo	8.2	AD 5 Occipital Ctx	8.4
Control 4 Hippo	25.2	AD 6 Occipital Ctx	18.6
Control (Path) 3 Hippo	4.4	Control 1 Occipital Ctx	2.4
AD 1 Temporal Ctx	21.9	Control 2 Occipital Ctx	18.2
AD 2 Temporal Ctx	21.8	Control 3 Occipital Ctx	32.1
AD 3 Temporal Ctx	15.1	Control 4 Occipital Ctx	2.2
AD 4 Temporal Ctx	29.7	Control (Path) 1 Occipital Ctx	64.2
AD 5 Inf Temporal Ctx	70.7	Control (Path) 2 Occipital Ctx	22.1
AD 5 Sup Temporal Ctx	41.5	Control (Path) 3 Occipital Ctx	8.4
AD 6 Inf Temporal Ctx	59.5	Control (Path) 4 Occipital Ctx	38.2
AD 6 Sup Temporal Ctx	53.2	Control 1 Parietal Ctx	10.5
Control 1 Temporal Ctx	17.8	Control 2 Parietal Ctx	42.3
Control 2 Temporal Ctx	17.0	Control 3 Parietal Ctx	16.3
Control 3 Temporal Ctx	15.3	Control (Path) 1 Parietal Ctx	56.3
Control 3 Temporal Ctx	16.6	Control (Path) 2 Parietal Ctx	17.9
Control (Path) 1 Temporal Ctx	47.0	Control (Path) 3 Parietal Ctx	7.3
Control (Path) 2 Temporal Ctx	44.1	Control (Path) 4 Parietal Ctx	69.3

Table ANC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3308, Run 215648361	Tissue Name	Rel. Exp.(%) Ag3308, Run 215648361
Adipose	13.4	Renal ca. TK-10	31.0
Melanoma* Hs688(A).T	4.6	Bladder	33.0
Melanoma* Hs688(B).T	4.0	Gastric ca. (liver met.) NCI-N87	57.0

Secondary Tr1 act	22.5	HUVEC TNF alpha + IFN gamma	9.2
Secondary Th1 rest	10.3	HUVEC TNF alpha + IL4	15.9
Secondary Th2 rest	7.4	HUVEC IL-11	9.9
Secondary Tr1 rest	20.3	Lung Microvascular EC none	9.2
Primary Th1 act	9.2	Lung Microvascular EC TNFalpha + IL-1beta	9.9
Primary Th2 act	16.6	Microvascular Dermal EC none	5.9
Primary Tr1 act	23.7	Microvascular Dermal EC TNFalpha + IL-1beta	11.7
Primary Th1 rest	82.4	Bronchial epithelium TNFalpha + IL1beta	19.1
Primary Th2 rest	50.7	Small airway epithelium none	7.9
Primary Tr1 rest	45.1	Small airway epithelium TNFalpha + IL-1beta	40.9
CD45RA CD4 lymphocyte act	19.9	Coronary artery SMC rest	7.5
CD45RO CD4 lymphocyte act	20.0	Coronary artery SMC TNFalpha + IL-1beta	0.7
CD8 lymphocyte act	8.2	Astrocytes rest	7.6
Secondary CD8 lymphocyte rest	24.3	Astrocytes TNFalpha + IL-1beta	0.8
Secondary CD8 lymphocyte act	18.3	KU-812 (Basophil) rest	37.6
CD4 lymphocyte none	9.8	KU-812 (Basophil) PMA/ionomycin	75.8
2ry Th1/Th2/Tr1_anti-CD95 CH11	28.3	CCD1106 (Keratinocytes) none	13.1
LAK cells rest	36.1	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	4.3
LAK cells IL-2	38.7	Liver cirrhosis	9.0
LAK cells IL-2+IL-12	36.3	Lupus kidney	10.9
LAK cells IL-2+IFN gamma	65.5	NCI-H292 none	36.1
LAK cells IL-2+ IL-18	30.1	NCI-H292 IL-4	56.3
LAK cells PMA/ionomycin	11.0	NCI-H292 IL-9	73.2
NK Cells IL-2 rest	25.0	NCI-H292 IL-13	28.9
Two Way MLR 3 day	31.9	NCI-H292 IFN gamma	31.2
Two Way MLR 5 day	19.9	HPAEC none	15.7
Two Way MLR 7 day	17.9	HPAEC TNF alpha + IL-1 beta	10.1
PBMC rest	28.9	Lung fibroblast none	5.2
PBMC PWM	58.2	Lung fibroblast TNF alpha + IL-1 beta	6.5
PBMC PHA-L	30.4	Lung fibroblast IL-4	3.7
Ramos (B cell) none	53.2	Lung fibroblast IL-9	11.8
Ramos (B cell) ionomycin	71.2	Lung fibroblast IL-13	4.0
B lymphocytes PWM	100.0	Lung fibroblast IFN gamma	17.3
B lymphocytes CD40L and IL-4	52.5	Dermal fibroblast CCD1070 rest	52.1
EOL-1 dbcAMP	17.8	Dermal fibroblast CCD1070 TNF alpha	78.5
EOL-1 dbcAMP PMA/ionomycin	19.6	Dermal fibroblast CCD1070 IL-1 beta	11.9
Dendritic cells none	10.2	Dermal fibroblast IFN gamma	4.3
Dendritic cells LPS	11.0	Dermal fibroblast IL-4	12.0
Dendritic cells anti-CD40	15.1	IBD Colitis 2	2.0
Monocytes rest	20.9	IBD Crohn's	2.4
Monocytes LPS	7.2	Colon	55.9

Macrophages rest	4.7	Lung	3.7
Macrophages LPS	0.0	Thymus	60.3
HUVEC none	16.4	Kidney	45.4
HUVEC starved	37.6		

CNS_neurodegeneration_v1.0 Summary: Ag3308 This panel confirms the expression of CG57678-01 gene at low levels in the brain in an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3308 Expression of CG57682-01 gene is highest in kidney (CT = 31.5). However, this gene is expressed at low to moderate levels across the majority of samples on this panel, suggesting that it may play a general role in cellular function and proliferation in a variety of cell types. The CG57682-01 gene encodes a protein with homology to G2/mitotic-specific cyclin B2.

This gene is expressed at low levels in several regions of the brain, including hippocampus, amygdala, cerebral cortex, thalamus, and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

Among tissues with metabolic or endocrine function, this gene is expressed at low levels in adrenal gland, pancreas, adipose, heart and skeletal muscle. Therefore, therapeutic modulation of the activity of this gene or its protein product may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

In addition, this gene is differentially expressed in fetal (CT = 34) as compared to adult liver (CT = 40) and may be useful for the identification of the fetal phenotype in this tissue.

Panel 4D Summary: Ag3308 CG57682-01 gene is expressed at highest levels in stimulated B lymphocytes (CT = 31.7). This gene is expressed at low levels in a wide range of cell types of significance in the immune response in health and disease. These cells include members of the T-cell, B-cell, endothelial cell, basophil, eosinophil, and peripheral blood mononuclear cell family, as well as epithelial and fibroblast cell types from lung and skin, and normal tissues represented by colon, thymus and kidney. This ubiquitous pattern of expression suggests that this gene product may be involved in homeostatic processes for these and other cell types and tissues.

This pattern is in agreement with the expression profile in General_screening_panel_v1.4 and also suggests a role for the gene product in cell survival and proliferation.

Therefore, therapeutic modulation of the activity of this gene or its protein product
5 may lead to the alteration of functions associated with these cell types and lead to
improvement of the symptoms of patients suffering from autoimmune and inflammatory
diseases such as asthma, allergies, inflammatory bowel disease, lupus erythematosus,
psoriasis, rheumatoid arthritis, and osteoarthritis.

NOV48

10 Expression of NOV48/CG57713-01 was assessed using the primer-probe set Ag3313, described in Table AOA. Results of the RTQ-PCR runs are shown in Tables AOB, AOC, AOD and AOE.

Table AOA. Probe Name Ag3313

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-agcatgtacatgtttcctttgc-3'	22	1162	401
Probe	TET-5'-atgcacttttcagctctgcagaagcg-3'-TAMRA	26	1187	402
Reverse	5'-tgcaacatttcacttccataca-3'	22	1238	403

Table AOB. CNS neurodegeneration v1.0

Tissue Name	Rel. Exp.(%) Ag3313, Run 210143317	Tissue Name	Rel. Exp.(%) Ag3313, Run 210143317
AD 1 Hippo	5.7	Control (Path) 3 Temporal Ctx	1.4
AD 2 Hippo	13.7	Control (Path) 4 Temporal Ctx	32.8
AD 3 Hippo	1.0	AD 1 Occipital Ctx	16.2
AD 4 Hippo	4.0	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	51.1	AD 3 Occipital Ctx	3.1
AD 6 Hippo	0.0	AD 4 Occipital Ctx	39.5
Control 2 Hippo	16.5	AD 5 Occipital Ctx	10.9
Control 4 Hippo	3.7	AD 6 Occipital Ctx	63.3
Control (Path) 3 Hippo	0.7	Control 1 Occipital Ctx	1.4
AD 1 Temporal Ctx	6.8	Control 2 Occipital Ctx	33.4
AD 2 Temporal Ctx	36.6	Control 3 Occipital Ctx	19.5
AD 3 Temporal Ctx	1.2	Control 4 Occipital Ctx	2.5
AD 4 Temporal Ctx	25.3	Control (Path) 1 Occipital Ctx	80.7
AD 5 Inf Temporal Ctx	100.0	Control (Path) 2 Occipital Ctx	14.5
AD 5 Sup Temporal Ctx	26.6	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	15.4	Control (Path) 4 Occipital Ctx	12.6
AD 6 Sup Temporal Ctx	30.4	Control 1 Parietal Ctx	10.1

Control 1 Temporal Ctx	2.2	Control 2 Parietal Ctx	37.1
Control 2 Temporal Ctx	34.4	Control 3 Parietal Ctx	14.7
Control 3 Temporal Ctx	18.2	Control (Path) 1 Parietal Ctx	63.7
Control 4 Temporal Ctx	11.1	Control (Path) 2 Parietal Ctx	32.3
Control (Path) 1 Temporal Ctx	58.2	Control (Path) 3 Parietal Ctx	1.9
Control (Path) 2 Temporal Ctx	49.7	Control (Path) 4 Parietal Ctx	52.1

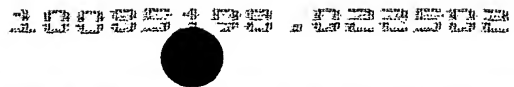
Table AOC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3313, Run 215648086	Tissue Name	Rel. Exp.(%) Ag3313, Run 215648086
Adipose	0.1	Renal ca. TK-10	0.2
Melanoma* Hs688(A).T	0.1	Bladder	0.3
Melanoma* Hs688(B).T	0.1	Gastric ca. (liver met.) NCI-N87	0.4
Melanoma* M14	1.5	Gastric ca. KATO III	0.1
Melanoma* LOXIMVI	0.1	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.1	Colon ca. SW480	0.2
Squamous cell carcinoma SCC-4	0.3	Colon ca. * (SW480 met) SW620	0.1
Testis Pool	0.6	Colon ca. HT29	0.1
Prostate ca. * (bone met) PC-3	0.2	Colon ca. HCT-116	30.1
Prostate Pool	0.2	Colon ca. CaCo-2	7.0
Placenta	0.3	Colon cancer tissue	0.3
Uterus Pool	0.0	Colon ca. SW1116	0.1
Ovarian ca. OVCAR-3	1.6	Colon ca. Colo-205	0.1
Ovarian ca. SK-OV-3	6.4	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	0.4	Colon Pool	0.3
Ovarian ca. OVCAR-5	0.4	Small Intestine Pool	0.5
Ovarian ca. IGROV-1	1.7	Stomach Pool	0.5
Ovarian ca. OVCAR-8	0.0	Bone Marrow Pool	0.6
Ovary	0.1	Fetal Heart	0.3
Breast ca. MCF-7	0.4	Heart Pool	0.1
Breast ca. MDA-MB-231	0.7	Lymph Node Pool	0.3
Breast ca. BT 549	3.1	Fetal Skeletal Muscle	0.4
Breast ca. T47D	0.4	Skeletal Muscle Pool	0.1
Breast ca. MDA-N	0.0	Spleen Pool	0.4
Breast Pool	0.2	Thymus Pool	0.9
Trachea	0.5	CNS cancer (glio/astro) U87-MG	0.3
Lung	0.1	CNS cancer (glio/astro) U-118-MG	0.3
Fetal Lung	0.5	CNS cancer (neuro;met) SK-N-AS	100.0
Lung ca. NCI-N417	1.9	CNS cancer (astro) SF-539	0.7
Lung ca. LX-1	0.4	CNS cancer (astro) SNB-75	1.0
Lung ca. NCI-H146	3.3	CNS cancer (glio) SNB-19	0.6
Lung ca. SHP-77	1.2	CNS cancer (glio) SF-295	0.5
Lung ca. A549	13.0	Brain (Amygdala) Pool	4.5
Lung ca. NCI-H526	0.4	Brain (cerebellum)	0.1
Lung ca. NCI-H23	5.6	Brain (fetal)	7.4
Lung ca. NCI-H460	2.9	Brain (Hippocampus) Pool	3.3

Lung ca. HOP-62	1.1	Cerebral Cortex Pool	2.9
Lung ca. NCI-H522	3.8	Brain (Substantia nigra) Pool	4.5
Liver	0.0	Brain (Thalamus) Pool	4.5
Fetal Liver	2.4	Brain (whole)	2.6
Liver ca. HepG2	0.0	Spinal Cord Pool	4.3
Kidney Pool	0.1	Adrenal Gland	2.0
Fetal Kidney	0.7	Pituitary gland Pool	5.9
Renal ca. 786-0	0.0	Salivary Gland	3.2
Renal ca. A498	0.0	Thyroid (female)	0.3
Renal ca. ACHN	0.3	Pancreatic ca. CAPAN2	0.8
Renal ca. UO-31	0.0	Pancreas Pool	0.2

Table AOD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3313, Run 164682847	Tissue Name	Rel. Exp.(%) Ag3313, Run 164682847
Secondary Th1 act	0.2	HUVEC IL-1beta	0.1
Secondary Th2 act	0.2	HUVEC IFN gamma	0.1
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.1
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.2	Lung Microvascular EC none	0.1
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.1
Primary Th2 act	0.1	Microvascular Dermal EC none	0.1
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.1
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.4	Small airway epithelium none	0.1
Primary Tr1 rest	0.1	Small airway epithelium TNFalpha + IL-1beta	0.4
CD45RA CD4 lymphocyte act	0.3	Coronary artery SMC rest	0.2
CD45RO CD4 lymphocyte act	0.1	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.1	Astrocytes rest	4.9
Secondary CD8 lymphocyte rest	0.1	Astrocytes TNFalpha + IL-1beta	0.9
Secondary CD8 lymphocyte act	0.3	KU-812 (Basophil) rest	81.2
CD4 lymphocyte none	0.1	KU-812 (Basophil) PMA/ionomycin	100.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.1	CCD1106 (Keratinocytes) none	0.3
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.1
LAK cells IL-2	0.0	Liver cirrhosis	0.2
LAK cells IL-2+IL-12	0.2	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.4	NCI-H292 none	0.2
LAK cells IL-2+ IL-18	0.3	NCI-H292 IL-4	0.6
LAK cells PMA/ionomycin	0.3	NCI-H292 IL-9	0.1
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.2	NCI-H292 IFN gamma	0.2
Two Way MLR 5 day	0.0	HPAEC none	0.1
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.1
PBMC rest	0.0	Lung fibroblast none	0.3



94723_Donor 2 U - C_Mesenchymal Stem Cells	0.0	73139_Uterus_Uterine smooth muscle cells	0.0
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CNS_neurodegeneration_v1.0 Summary: Ag3313 This panel confirms the expression of CG57713-01 gene at low to moderate levels in the brains of an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3313 Expression of the CG57713-01 gene is highest in CNS cancer cell line SK-N-AS (CT = 26.1). Expression of this gene also appears to be upregulated in a number of lung cancer cell lines and ovarian cancer cell lines when compared to the normal tissues. Therefore, therapeutic modulation of the activity of this gene or its protein product may be of use in the treatment of lung or ovarian cancer.

In addition, this gene is expressed at moderate levels in most regions of the central nervous system examined, including amygdala, hippocampus, cerebral cortex, substantia nigra, thalamus and spinal cord. The CG57713-01 gene encodes a protein with homology to sodium/bile acid cotransporters. Changes in expression of sodium/bile acid cotransporters have been found to be associated with methamphetamine (METH)-induced dopamine (DA) neurotoxicity (ref. 1). In addition, based on the expression of the CG57713-01 gene in the brain, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

Among tissues with metabolic or endocrine function, this gene is expressed at moderate levels in adrenal gland and pituitary gland and at low levels in pancreas, thyroid, fetal heart, fetal skeletal muscle, and fetal liver. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes. Interestingly, expression of this gene is much higher in fetal liver (CT = 31.5) than in adult liver (CT = 40), suggesting that expression of this gene can be used to distinguish these two tissues.

References:

1. Xie T, Tong L, Barrett T, Yuan J, Hatzidimitriou G, McCann UD, Becker KG, Donovan DM, Ricaurte GA. Changes in gene expression linked to methamphetamine induced dopaminergic neurotoxicity. J Neurosci 2002 Jan 1;22(1):274-83

The purpose of these studies was to examine the role of gene expression in methamphetamine (METH)-induced dopamine (DA) neurotoxicity. First, the effects of the mRNA synthesis inhibitor, actinomycin-D, and the protein synthesis inhibitor, cycloheximide, were examined. Both agents afforded complete protection against METH-induced DA neurotoxicity and did so independently of effects on core temperature, DA transporter function, or METH brain levels, suggesting that gene transcription and mRNA translation play a role in METH neurotoxicity. Next, microarray technology, in combination with an experimental approach designed to facilitate recognition of relevant gene expression patterns, was used to identify gene products linked to METH-induced DA neurotoxicity. This led to the identification of several genes in the ventral midbrain associated with the neurotoxic process, including genes for energy metabolism [cytochrome c oxidase subunit 1 (COX1), reduced nicotinamide adenine dinucleotide ubiquinone oxidoreductase chain 2, and phosphoglycerate mutase B], ion regulation (members of sodium/hydrogen exchanger and sodium/bile acid cotransporter family), signal transduction (adenylyl cyclase III), and cell differentiation and degeneration (N-myc downstream-regulated gene 3 and tau protein). Of these differentially expressed genes, we elected to further examine the increase in COX1 expression, because of data implicating energy utilization in METH neurotoxicity and the known role of COX1 in energy metabolism. On the basis of time course studies, Northern blot analyses, in situ hybridization results, and temperature studies, we now report that increased COX1 expression in the ventral midbrain is linked to METH induced DA neuronal injury. The precise role of COX1 and other genes in METH neurotoxicity remains to be elucidated.

PMID: 11756511

Panel 4D Summary: Ag3313 The CG57713-01 transcript is expressed at highest levels in both PMA/ionomycin-treated KU-812 basophil cell line and in untreated KU-812 cells (CTs = 28). Therefore, expression of this gene can be used to distinguish basophils from the other samples on this panel. In addition, small molecule therapies designed with the protein encoded for by this gene could block or inhibit inflammation or tissue damage due to basophil activation in response to asthma, allergies, hypersensitivity reactions, psoriasis, and viral infections.

In addition, expression of this gene is higher in normal colon (CT = 32.9) than in colon samples from patients with IBD Crohn's (CT = 36) or IBD colitis (CT = 37). The CG57713-01 gene encodes a protein with homology to sodium/bile acid cotransporters. Defects in the sodium/bile acid cotransporter are one of the causative agents for Crohn's disease (Ref 1).

Thus, therapeutic modulation of this novel cotransporter may be of use in the treatment of Crohn's disease.

References.

1. Wong MH, Oelkers P, Dawson PA. (1995) Identification of a mutation in the ileal sodium-dependent bile acid transporter gene that abolishes transport activity. J Biol Chem. 270(45):27228-34.

The ileal Na⁺/bile acid cotransporter plays a critical role in the reabsorption of bile acids from the small intestine. In the course of cloning and characterizing the human ileal Na⁺/bile acid cotransporter cDNA, a dysfunctional isoform was identified in a patient diagnosed with Crohn's disease. Expression studies using hamster-human ileal Na⁺/bile acid cotransporter cDNA chimeras narrowed the location of the defect to the carboxyl-terminal 94 amino acids. Comparison of the sequence of the dysfunctional isoform to that of a wild-type human ileal Na⁺/bile acid cotransporter genomic clone revealed a single C to T transition resulting in a proline to serine substitution at amino acid position 290. The inheritance of this mutation in the proband's family was confirmed by single-stranded conformation polymorphism analysis and DNA sequencing. In transfected COS-1 cells, the single amino acid change abolished taurocholate transport activity but did not alter the transporter's synthesis or subcellular distribution. This dysfunctional mutation represents the first known molecular defect in a human sodium-dependent bile acid transporter.

PMID: 7592981

Panel 5 Islet Summary: Ag3313 A low level of expression of the CG57713-01 gene is seen in a sample derived from small intestine (CT=34), which is confirmed by the expression observed in panel 1.4. Defects in the sodium/bile acid cotransporter are one of the causative agent for Crohn's disease (Ref 1). Thus, therapeutic modulation of this novel cotransporter may be of use in the treatment of Crohn's disease.

References.

1. Wong MH, Oelkers P, Dawson PA. (1995) Identification of a mutation in the ileal sodium-dependent bile acid transporter gene that abolishes transport activity. J Biol Chem. 270(45):27228-34.

The ileal Na⁺/bile acid cotransporter plays a critical role in the reabsorption of bile acids from the small intestine. In the course of cloning and characterizing the human ileal Na⁺/bile acid cotransporter cDNA, a dysfunctional isoform was identified in a patient

diagnosed with Crohn's disease. Expression studies using hamster-human ileal Na⁺/bile acid cotransporter cDNA chimeras narrowed the location of the defect to the carboxyl-terminal 94 amino acids. Comparison of the sequence of the dysfunctional isoform to that of a wild-type human ileal Na⁺/bile acid cotransporter genomic clone revealed a single C to T transition
 5 resulting in a proline to serine substitution at amino acid position 290. The inheritance of this mutation in the proband's family was confirmed by single-stranded conformation polymorphism analysis and DNA sequencing. In transfected COS-1 cells, the single amino acid change abolished taurocholate transport activity but did not alter the transporter's synthesis or subcellular distribution. This dysfunctional mutation represents the first known
 10 molecular defect in a human sodium-dependent bile acid transporter.

PMID: 7592981

NOV49

Expression of NOV49/CG57721-01 was assessed using the primer-probe set Ag3315, described in Table APA. Results of the RTQ-PCR runs are shown in Tables APB, APC and
 15 APD.

Table APA. Probe Name Ag3315

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-atctacctctccgagtcctca-3'	22	652	404
Probe	TET-5'-ctgcagatcctgattcggtgctcaa-3'-TAMRA	26	700	405
Reverse	5'-gatggtcagtcggaagatgtac-3'	22	726	406

Table APB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3315, Run 210138297	Tissue Name	Rel. Exp.(%) Ag3315, Run 210138297
AD 1 Hippo	17.1	Control (Path) 3 Temporal Ctx	4.9
AD 2 Hippo	0.0	Control (Path) 4 Temporal Ctx	13.5
AD 3 Hippo	6.4	AD 1 Occipital Ctx	7.0
AD 4 Hippo	37.6	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	12.7	AD 3 Occipital Ctx	0.0
AD 6 Hippo	92.7	AD 4 Occipital Ctx	17.1
Control 2 Hippo	0.0	AD 5 Occipital Ctx	31.6
Control 4 Hippo	18.3	AD 6 Occipital Ctx	11.6
Control (Path) 3 Hippo	0.0	Control 1 Occipital Ctx	0.0
AD 1 Temporal Ctx	0.0	Control 2 Occipital Ctx	18.9
AD 2 Temporal Ctx	0.0	Control 3 Occipital Ctx	0.0
AD 3 Temporal Ctx	0.0	Control 4 Occipital Ctx	12.2
AD 4 Temporal Ctx	29.5	Control (Path) 1 Occipital Ctx	40.6
AD 5 Inf Temporal Ctx	11.7	Control (Path) 2 Occipital Ctx	9.3

AD 5 SupTemporal Ctx	30.6	Control (Path) 3 Occipital Ctx	5.2
AD 6 Inf Temporal Ctx	80.7	Control (Path) 4 Occipital Ctx	19.2
AD 6 Sup Temporal Ctx	100.0	Control 1 Parietal Ctx	0.0
Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	29.7
Control 2 Temporal Ctx	5.5	Control 3 Parietal Ctx	14.4
Control 3 Temporal Ctx	5.0	Control (Path) 1 Parietal Ctx	11.5
Control 4 Temporal Ctx	13.8	Control (Path) 2 Parietal Ctx	5.5
Control (Path) 1 Temporal Ctx	31.4	Control (Path) 3 Parietal Ctx	0.0
Control (Path) 2 Temporal Ctx	24.1	Control (Path) 4 Parietal Ctx	11.3

Table APC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3315, Run 215678587	Tissue Name	Rel. Exp.(%) Ag3315, Run 215678587
Adipose	0.2	Renal ca. TK-10	0.3
Melanoma* Hs688(A).T	0.0	Bladder	2.2
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	12.7
Melanoma* M14	0.0	Gastric ca. KATO III	100.0
Melanoma* LOXIMVI	0.1	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	7.1
Squamous cell carcinoma SCC-4	0.1	Colon ca.* (SW480 met) SW620	0.0
Testis Pool	0.1	Colon ca. HT29	0.9
Prostate ca.* (bone met) PC-3	0.0	Colon ca. HCT-116	0.0
Prostate Pool	0.0	Colon ca. CaCo-2	0.1
Placenta	0.0	Colon cancer tissue	0.4
Uterus Pool	0.1	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.4	Colon ca. Colo-205	13.3
Ovarian ca. SK-OV-3	0.2	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	0.2	Colon Pool	0.1
Ovarian ca. OVCAR-5	6.6	Small Intestine Pool	0.2
Ovarian ca. IGROV-1	3.2	Stomach Pool	6.7
Ovarian ca. OVCAR-8	0.1	Bone Marrow Pool	0.0
Ovary	0.9	Fetal Heart	0.1
Breast ca. MCF-7	0.2	Heart Pool	0.1
Breast ca. MDA-MB-231	0.2	Lymph Node Pool	0.2
Breast ca. BT 549	0.2	Fetal Skeletal Muscle	0.0
Breast ca. T47D	7.3	Skeletal Muscle Pool	0.4
Breast ca. MDA-N	0.0	Spleen Pool	0.0
Breast Pool	0.0	Thymus Pool	0.1
Trachea	3.3	CNS cancer (glio/astro) U87-MG	0.2
Lung	0.1	CNS cancer (glio/astro) U-118-MG	0.0
Fetal Lung	6.0	CNS cancer (neuro;met) SK-N-AS	0.0
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.1
Lung ca. LX-1	0.6	CNS cancer (astro) SNB-75	0.2
Lung ca. NCI-H146	0.0	CNS cancer (glio) SNB-19	2.6

Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	0.2
Lung ca. A549	1.4	Brain (Amygdala) Pool	0.0
Lung ca. NCI-H526	0.1	Brain (cerebellum)	0.0
Lung ca. NCI-H23	0.0	Brain (fetal)	0.2
Lung ca. NCI-H460	0.1	Brain (Hippocampus) Pool	0.0
Lung ca. HOP-62	0.3	Cerebral Cortex Pool	0.1
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	0.2
Liver	0.0	Brain (Thalamus) Pool	0.1
Fetal Liver	0.1	Brain (whole)	0.1
Liver ca. HepG2	0.5	Spinal Cord Pool	0.3
Kidney Pool	0.2	Adrenal Gland	0.0
Fetal Kidney	0.1	Pituitary gland Pool	0.1
Renal ca. 786-0	0.1	Salivary Gland	79.6
Renal ca. A498	0.1	Thyroid (female)	1.5
Renal ca. ACHN	0.1	Pancreatic ca. CAPAN2	7.2
Renal ca. UO-31	0.1	Pancreas Pool	0.7

Table APD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3315, Run 164683047	Tissue Name	Rel. Exp.(%) Ag3315, Run 164683047
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	1.3
Secondary Th2 rest	1.4	HUVEC IL-11	3.8
Secondary Tr1 rest	1.5	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	2.7
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	2.9
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	2.8
Primary Th2 rest	0.0	Small airway epithelium none	4.1
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	100.0
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	1.4
CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	1.6	KU-812 (Basophil) rest	2.8
CD4 lymphocyte none	1.7	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1 _anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	3.1
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	1.5
LAK cells PMA/ionomycin	1.4	NCI-H292 IL-9	2.1

protein. Prestin has been demonstrated to act as a motor protein of cochlear outer hair cells and presumably plays an important role in hearing (Ref. 1, 2). Based on the similarity of the CG57721-01 gene to prestin, therapeutic modulation of the activity of this gene or its protein product may be of benefit in the treatment of deafness.

5 Finally, among tissues with metabolic or endocrine function, this gene is expressed at low levels in pancreas, thyroid, skeletal muscle, and adipose. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes. This gene is expressed in the thyroid and is also similar to the pendrin gene. Mutations in the pendrin gene are
10 known to cause the human disease Pendred syndrome (Ref. 3). Therefore, therapeutic modulation of this gene may be useful in treatment of Pendred syndrome and related disorders.

References:

1. Zheng J, Shen W, He DZ, Long KB, Madison LD, Dallos P. (2000) Prestin is the motor protein of cochlear outer hair cells. *Nature* 405(6783):149-55

15 The outer and inner hair cells of the mammalian cochlea perform different functions. In response to changes in membrane potential, the cylindrical outer hair cell rapidly alters its length and stiffness. These mechanical changes, driven by putative molecular motors, are assumed to produce amplification of vibrations in the cochlea that are transduced by inner hair cells. Here we have identified an abundant complementary DNA from a gene, designated
20 Prestin, which is specifically expressed in outer hair cells. Regions of the encoded protein show moderate sequence similarity to pendrin and related sulphate/anion transport proteins. Voltage-induced shape changes can be elicited in cultured human kidney cells that express prestin. The mechanical response of outer hair cells to voltage change is accompanied by a 'gating current', which is manifested as nonlinear capacitance. We also demonstrate this
25 nonlinear capacitance in transfected kidney cells. We conclude that prestin is the motor protein of the cochlear outer hair cell.

PMID: 10821263

2. Peter Dallos & Bernd Fakler (2002) Prestin, a new type of motor protein. *Nature Reviews Molecular Cell Biology* 3, 104 -111.

30 Prestin, a transmembrane protein found in the outer hair cells of the cochlea, represents a new type of molecular motor, which is likely to be of great interest to molecular cell biologists. In contrast to enzymatic-activity-based motors, prestin is a direct voltage-to-force converter, which uses cytoplasmic anions as extrinsic voltage sensors and can operate at

microsecond rates. As prestin mediates changes in outer hair cell length in response to membrane potential variations, it might be responsible for sound amplification in the mammalian hearing organ.

3. Waldegger S, Moschen I, Ramirez A, Smith RJ, Ayadi H, Lang F, Kubisch C.
5 (2001) Cloning and characterization of SLC26A6, a novel member of the solute carrier 26 gene family. Genomics. 72(1):43-50.

The SLC26 gene family (solute carrier family 26) comprises five mammalian genes that encode anion transporter-related proteins. In addition to sat-1 and prestin, which were cloned from rat and gerbil, respectively, three human members have been identified and
10 associated with specific genetic diseases (DTD, diastrophic dysplasia; CLD, congenital chloride diarrhea; PDS, Pendred syndrome). In this study we used a homology approach combined with RACE PCR to identify human SLC26A6, the sixth member of this gene family. Northern blot analysis showed the highest SLC26A6 transcript levels in kidney and pancreas. Expression in MDCK cells and in *Xenopus* oocytes demonstrated trafficking of the
15 SLC26A6 protein to the cell membrane but did not reveal anion transport activity with tracer uptake or intracellular pH measurements. We determined the genomic structure of the SLC26A6 gene and excluded mutations in the 21 coding exons as the cause of DFNB6 and USH2B, which closely map to the SLC26A6 chromosomal locus (3p21).

PMID: 11247665

20 **Panel 4D Summary:** Ag3315 Expression of the CG57721-01 gene is limited to small airway epithelium (CT = 35) and normal lung (CT = 31.7) on this panel. Interestingly, expression of this gene in small airway epithelium is strongly upregulated by treatment with TNF-alpha and IL-1 beta (CT = 30.4). This observation suggests that expression of this gene could be used as a marker for activated epithelium. Furthermore, therapeutic modulation of the
25 activity of this gene or its protein product using small molecule drugs could be of use in the treatment of asthma and emphysema.

NOV50

Expression of NOV50/CG57787-01 was assessed using the primer-probe sets Ag3332, Ag2005 and Ag2259, described in Tables AQA, AQB and AQC. Results of the RTQ-PCR
30 runs are shown in Tables AQD, AQE, AQF and AQG.

Table AQA. Probe Name Ag3332

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-atttctaccccgctcattaaag-3'	22	67	407
Probe	TET-5'-caccatcggttgacagatcaag-3'-TAMRA	25	111	408
Reverse	5'-gttctgtagtcacagcagggtt-3'	21	136	409

Table AQB. Probe Name Ag2005

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gttctgtgctggacttcatttc-3'	21	51	410
Probe	TET-5'-accccgctcattaaaggcttcacctct-3'-TAMRA	26	74	411
Reverse	5'-cagggtctgtgatctgtccaaag-3'	22	120	412

Table AQC. Probe Name Ag2259

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gttctgtgctggacttcatttc-3'	21	51	413
Probe	TET-5'-accccgctcattaaaggcttcacctct-3'-TAMRA	26	74	414
Reverse	5'-cagggtctgtgatctgtccaaag-3'	22	120	415

Table AOD. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3332, Run 210146364	Tissue Name	Rel. Exp.(%) Ag3332, Run 210146364
AD 1 Hippo	16.4	Control (Path) 3 Temporal Ctx	3.9
AD 2 Hippo	56.6	Control (Path) 4 Temporal Ctx	44.4
AD 3 Hippo	7.1	AD 1 Occipital Ctx	15.6
AD 4 Hippo	13.2	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	97.3	AD 3 Occipital Ctx	5.7
AD 6 Hippo	59.0	AD 4 Occipital Ctx	28.9
Control 2 Hippo	40.9	AD 5 Occipital Ctx	27.5
Control 4 Hippo	23.7	AD 6 Occipital Ctx	88.3
Control (Path) 3 Hippo	8.7	Control 1 Occipital Ctx	2.6
AD 1 Temporal Ctx	18.7	Control 2 Occipital Ctx	53.6
AD 2 Temporal Ctx	45.1	Control 3 Occipital Ctx	19.1
AD 3 Temporal Ctx	9.9	Control 4 Occipital Ctx	9.9
AD 4 Temporal Ctx	40.9	Control (Path) 1 Occipital Ctx	81.8
AD 5 Inf Temporal Ctx	100.0	Control (Path) 2 Occipital Ctx	9.5
AD 5 Sup Temporal Ctx	87.1	Control (Path) 3 Occipital Ctx	3.4
AD 6 Inf Temporal Ctx	62.4	Control (Path) 4 Occipital Ctx	16.5
AD 6 Sup Temporal Ctx	62.0	Control 1 Parietal Ctx	6.6
Control 1 Temporal Ctx	5.3	Control 2 Parietal Ctx	83.5
Control 2 Temporal Ctx	46.7	Control 3 Parietal Ctx	17.8
Control 3 Temporal Ctx	31.6	Control (Path) 1 Parietal Ctx	99.3
Control 4 Temporal Ctx	14.7	Control (Path) 2 Parietal Ctx	19.9
Control (Path) 1 Temporal Ctx	84.1	Control (Path) 3 Parietal Ctx	3.7
Control (Path) 2 Temporal Ctx	41.8	Control (Path) 4 Parietal Ctx	47.3

Table AQE. General_screening_panel_v1.4

Tissue Name	Tissue Name
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	215678734		215678734
Adipose	6.6	Renal ca. TK-10	100.0
Melanoma* Hs688(A).T	28.5	Bladder	18.0
Melanoma* Hs688(B).T	31.0	Gastric ca. (liver met.) NCI-N87	17.1
Melanoma* M14	30.4	Gastric ca. KATO III	19.3
Melanoma* LOXIMVI	22.5	Colon ca. SW-948	9.0
Melanoma* SK-MEL-5	30.1	Colon ca. SW480	0.7
Squamous cell carcinoma SCC-4	0.2	Colon ca.* (SW480 met) SW620	1.9
Testis Pool	5.3	Colon ca. HT29	4.9
Prostate ca.* (bone met) PC-3	53.6	Colon ca. HCT-116	28.9
Prostate Pool	12.7	Colon ca. CaCo-2	49.0
Placenta	55.9	Colon cancer tissue	12.9
Uterus Pool	3.7	Colon ca. SW1116	6.8
Ovarian ca. OVCAR-3	42.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	40.6	Colon ca. SW-48	16.7
Ovarian ca. OVCAR-4	19.9	Colon Pool	26.6
Ovarian ca. OVCAR-5	57.0	Small Intestine Pool	46.0
Ovarian ca. IGROV-1	30.4	Stomach Pool	13.7
Ovarian ca. OVCAR-8	9.7	Bone Marrow Pool	5.9
Ovary	18.3	Fetal Heart	14.0
Breast ca. MCF-7	35.1	Heart Pool	10.0
Breast ca. MDA-MB-231	19.5	Lymph Node Pool	16.8
Breast ca. BT 549	37.4	Fetal Skeletal Muscle	4.2
Breast ca. T47D	97.3	Skeletal Muscle Pool	6.9
Breast ca. MDA-N	13.6	Spleen Pool	17.7
Breast Pool	22.7	Thymus Pool	14.8
Trachea	21.0	CNS cancer (glio/astro) U87-MG	9.0
Lung	4.0	CNS cancer (glio/astro) U-118-MG	24.7
Fetal Lung	53.2	CNS cancer (neuro;met) SK-N-AS	79.6
Lung ca. NCI-N417	0.9	CNS cancer (astro) SF-539	3.7
Lung ca. LX-1	0.8	CNS cancer (astro) SNB-75	54.7
Lung ca. NCI-H146	12.4	CNS cancer (glio) SNB-19	24.0
Lung ca. SHP-77	24.3	CNS cancer (glio) SF-295	58.6
Lung ca. A549	33.9	Brain (Amygdala) Pool	13.9
Lung ca. NCI-H526	20.0	Brain (cerebellum)	14.9
Lung ca. NCI-H23	30.4	Brain (fetal)	40.3
Lung ca. NCI-H460	34.9	Brain (Hippocampus) Pool	25.5
Lung ca. HOP-62	4.0	Cerebral Cortex Pool	23.8
Lung ca. NCI-H522	72.2	Brain (Substantia nigra) Pool	35.4
Liver	5.0	Brain (Thalamus) Pool	29.9
Fetal Liver	17.4	Brain (whole)	10.6
Liver ca. HepG2	26.4	Spinal Cord Pool	24.8
Kidney Pool	35.6	Adrenal Gland	65.1
Fetal Kidney	14.6	Pituitary gland Pool	17.0
Renal ca. 786-0	0.9	Salivary Gland	11.6
Renal ca. A498	16.4	Thyroid (female)	17.9
Renal ca. ACHN	11.4	Pancreatic ca. CAPAN2	2.4
Renal ca. UO-31	4.6	Pancreas Pool	21.0

Table AQF. Panel I.3D

Tissue Name	Rel. Exp.(%) Ag2005, Run 165981814	Tissue Name	Rel. Exp.(%) Ag2005, Run 165981814
Liver adenocarcinoma	36.6	Kidney (fetal)	33.2
Pancreas	14.4	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.9	Renal ca. A498	12.8
Adrenal gland	46.3	Renal ca. RXF 393	20.9
Thyroid	9.6	Renal ca. ACHN	3.3
Salivary gland	20.7	Renal ca. UO-31	5.4
Pituitary gland	58.2	Renal ca. TK-10	40.1
Brain (fetal)	28.7	Liver	3.1
Brain (whole)	92.7	Liver (fetal)	10.7
Brain (amygdala)	78.5	Liver ca. (hepatoblast) HepG2	15.6
Brain (cerebellum)	12.7	Lung	27.9
Brain (hippocampus)	53.2	Lung (fetal)	53.2
Brain (substantia nigra)	52.1	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	90.8	Lung ca. (small cell) NCI- H69	6.6
Cerebral Cortex	100.0	Lung ca. (s.cell var.) SHP- 77	22.4
Spinal cord	56.6	Lung ca. (large cell) NCI- H460	15.9
glio/astro U87-MG	6.0	Lung ca. (non-sm. cell) A549	9.8
glio/astro U-118-MG	7.6	Lung ca. (non-s.cell) NCI- H23	13.7
astrocytoma SW1783	6.4	Lung ca. (non-s.cell) HOP- 62	8.4
neuro*; met SK-N-AS	26.8	Lung ca. (non-s.cl) NCI- H522	15.8
astrocytoma SF-539	3.1	Lung ca. (squam.) SW 900	28.1
astrocytoma SNB-75	12.9	Lung ca. (squam.) NCI- H596	2.6
glioma SNB-19	13.1	Mammary gland	10.5
glioma U251	8.2	Breast ca. * (pl.ef) MCF-7	14.8
glioma SF-295	19.3	Breast ca. * (pl.ef) MDA- MB-231	10.4
Heart (fetal)	28.5	Breast ca. * (pl.ef) T47D	28.7
Heart	4.8	Breast ca. BT-549	5.3
Skeletal muscle (fetal)	16.5	Breast ca. MDA-N	3.6
Skeletal muscle	13.9	Ovary	39.2
Bone marrow	2.6	Ovarian ca. OVCAR-3	11.4
Thymus	16.4	Ovarian ca. OVCAR-4	51.4
Spleen	23.5	Ovarian ca. OVCAR-5	20.4
Lymph node	37.4	Ovarian ca. OVCAR-8	12.2
Colorectal	12.4	Ovarian ca. IGROV-1	12.2
Stomach	14.6	Ovarian ca. * (ascites) SK- OV-3	15.5
Small intestine	18.6	Uterus	20.3
Colon ca. SW480	0.0	Placenta	71.2
Colon ca. * SW620(SW480 met)	1.5	Prostate	14.1
Colon ca. HT29	0.7	Prostate ca. * (bone met) PC- 3	22.7
Colon ca. HCT-116	6.8	Testis	8.6

Colon ca. CaCo-2	13.7	Melanoma Hs688(A).T	11.7
Colon ca. tissue(ODO3866)	13.5	Melanoma* (met) Hs688(B).T	8.8
Colon ca. HCC-2998	18.2	Melanoma UACC-62	28.7
Gastric ca.* (liver met) NCI-N87	9.7	Melanoma M14	17.4
Bladder	6.8	Melanoma LOX IMV1	2.6
Trachea	6.3	Melanoma* (met) SK-MEL-5	16.6
Kidney	28.7	Adipose	5.6

Table AQG. Panel 4D

Tissue Name	Rel. Exp.(%) Ag2259, Run 150910665	Rel. Exp.(%) Ag3332, Run 165725931	Tissue Name	Rel. Exp.(%) Ag2259, Run 150910665	Rel. Exp.(%) Ag3332, Run 165725931
Secondary Th1 act	3.1	2.7	HUVEC IL-1beta	1.9	1.2
Secondary Th2 act	2.4	1.2	HUVEC IFN gamma	8.5	3.5
Secondary Tr1 act	6.6	6.7	HUVEC TNF alpha + IFN gamma	3.5	1.5
Secondary Th1 rest	1.8	2.8	HUVEC TNF alpha + IL4	3.8	1.4
Secondary Th2 rest	4.5	4.1	HUVEC IL-11	2.2	1.7
Secondary Tr1 rest	2.5	2.9	Lung Microvascular EC none	6.8	2.5
Primary Th1 act	1.0	0.4	Lung Microvascular EC TNFalpha + IL-1beta	4.7	2.1
Primary Th2 act	3.2	2.7	Microvascular Dermal EC none	3.5	2.5
Primary Tr1 act	1.2	0.9	Microvascular Dermal EC TNFalpha + IL- 1beta	3.0	2.1
Primary Th1 rest	2.0	2.0	Bronchial epithelium TNFalpha + IL1beta	1.7	1.1
Primary Th2 rest	3.3	2.4	Small airway epithelium none	1.4	0.3
Primary Tr1 rest	2.0	1.3	Small airway epithelium TNFalpha + IL-1beta	1.6	0.8
CD45RA CD4 lymphocyte act	2.0	1.3	Coronary artery SMC rest	2.3	1.4
CD45RO CD4 lymphocyte act	3.3	2.4	Coronary artery SMC TNFalpha + IL-1beta	2.3	1.1
CD8 lymphocyte act	2.6	1.5	Astrocytes rest	0.4	0.8
Secondary CD8 lymphocyte rest	6.1	6.1	Astrocytes TNFalpha + IL-1beta	1.6	2.6
Secondary CD8 lymphocyte act	0.3	0.6	KU-812 (Basophil) rest	0.0	0.0
CD4 lymphocyte none	5.6	5.3	KU-812 (Basophil) PMA/ionomycin	0.2	0.0
2ry Th1/Th2/Tr1_anti- CD95 CH11	1.9	2.5	CCD1106 (Keratinocytes) none	0.7	0.4
LAK cells rest	25.5	17.2	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	1.1	3.4
LAK cells IL-2	3.8	3.9	Liver cirrhosis	1.2	1.9
LAK cells IL-2+IL-12	15.0	8.8	Lupus kidney	1.1	3.3
LAK cells IL-2+IFN gamma	16.2	13.8	NCI-H292 none	4.5	2.2
LAK cells IL-2+ IL- 18	12.6	7.9	NCI-H292 IL-4	8.0	3.7

LAK cells PMA/ionomycin	15.7	12.7	NCI-H292 IL-9	6.4	4.5
NK Cells IL-2 rest	5.4	2.9	NCI-H292 IL-13	4.5	2.6
Two Way MLR 3 day	14.7	9.9	NCI-H292 IFN gamma	3.3	1.4
Two Way MLR 5 day	9.6	7.3	HPAEC none	6.4	3.7
Two Way MLR 7 day	2.5	1.5	HPAEC TNF alpha + IL-1 beta	8.8	5.3
PBMC rest	3.5	4.3	Lung fibroblast none	6.7	10.1
PBMC PWM	14.3	4.1	Lung fibroblast TNF alpha + IL-1 beta	3.7	9.4
PBMC PHA-L	2.4	0.7	Lung fibroblast IL-4	13.3	5.6
Ramos (B cell) none	0.0	0.1	Lung fibroblast IL-9	8.5	4.7
Ramos (B cell) ionomycin	0.2	0.0	Lung fibroblast IL-13	8.7	4.2
B lymphocytes PWM	3.7	0.7	Lung fibroblast IFN gamma	9.0	5.1
B lymphocytes CD40L and IL-4	10.2	3.0	Dermal fibroblast CCD1070 rest	4.6	2.3
EOL-1 dbcAMP	4.2	2.9	Dermal fibroblast CCD1070 TNF alpha	4.2	3.1
EOL-1 dbcAMP PMA/ionomycin	4.3	4.5	Dermal fibroblast CCD1070 IL-1 beta	3.7	1.3
Dendritic cells none	77.4	74.7	Dermal fibroblast IFN gamma	3.5	1.8
Dendritic cells LPS	30.4	19.3	Dermal fibroblast IL-4	6.7	4.1
Dendritic cells anti- CD40	95.3	100.0	IBD Colitis 2	0.6	0.5
Monocytes rest	7.0	3.3	IBD Crohn's	0.5	0.6
Monocytes LPS	18.8	18.4	Colon	4.2	11.0
Macrophages rest	100.0	89.5	Lung	4.5	3.1
Macrophages LPS	15.2	10.2	Thymus	13.8	6.1
HUVEC none	3.5	2.4	Kidney	3.9	1.9
HUVEC starved	7.7	6.8			

CNS_neurodegeneration_v1.0 Summary: Ag3332 This panel confirms the expression of the CG57787-01 gene at moderate levels in the brains of an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3332 Expression of the CG57787-01 gene is highest in renal cell carcinoma cell line TK-10 (CT = 28.3). In addition, levels of expression of this gene are higher in fetal lung (CT=29) and 7 lung cancer cell lines than in the adult lung (CT=33). Thus, expression of this gene could be used to differentiate adult and fetal lung and also as marker to detect the presence of lung cancer. Furthermore, therapeutic modulation of the expression or function of this gene may be effective in the treatment of lung cancer.

In addition, this gene is expressed at moderate levels throughout the central nervous system, including in amygdala, cerebellum, hippocampus, cerebral cortex, substantia nigra, thalamus and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

Among tissues with metabolic or endocrine function, this gene is expressed at moderate levels in pancreas, adrenal gland, pituitary gland, adipose, thyroid, skeletal muscle, heart, and liver. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

Panel 1.3D Summary: Ag3332 Expression of the CG57787-01 gene is highest in cerebral cortex (CT = 31.2). In addition, this gene is expressed at moderate levels throughout the central nervous system, including in amygdala, cerebellum, hippocampus, cerebral cortex, substantia nigra, thalamus and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

Among tissues with metabolic or endocrine function, this gene is expressed at moderate levels in pancreas, adrenal gland, pituitary gland, adipose, thyroid, skeletal muscle, heart, and liver. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

Panel 4D Summary: Ag2259/Ag3332 Results from two experiments using different probe/primer sets are in excellent agreement. Expression of the CG57787-01 gene is highest in treated and untreated dendritic cells and macrophages. Dendritic cells and macrophages are powerful antigen-presenting cells (APC) whose function is pivotal in the initiation and maintenance of normal immune responses. Autoimmunity and inflammation may also be reduced by suppression of this function. Therefore, therapeutic utilization of the protein encoded by this transcript may be important in the treatment of diseases where antigen presentation, a function of mature dendritic cells, plays an important role, such as asthma, rheumatoid arthritis, IBD, and psoriasis.

AR. CG57785-01: Sulfate transporter

Expression of gene CG57785-01 was assessed using the primer-probe set Ag3331, described in Table ARA. Results of the RTQ-PCR runs are shown in Tables ARB, ARC and ARD.

Table ARA. Probe Name Ag3331

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ctcatatttctgggcaagaaga-3'	22	646	416
Probe	TET-5'-tgccagtcctcacaattacagtgtca-3'-TAMRA	26	669	417
Reverse	5'-cgatggctattaatcctggtt-3'	22	700	418

5 Table ARB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3331, Run 210146363	Tissue Name	Rel. Exp.(%) Ag3331, Run 210146363
AD 1 Hippo	15.5	Control (Path) 3 Temporal Ctx	4.5
AD 2 Hippo	39.2	Control (Path) 4 Temporal Ctx	57.0
AD 3 Hippo	3.3	AD 1 Occipital Ctx	24.7
AD 4 Hippo	6.3	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	84.7	AD 3 Occipital Ctx	0.0
AD 6 Hippo	40.9	AD 4 Occipital Ctx	18.4
Control 2 Hippo	35.6	AD 5 Occipital Ctx	82.4
Control 4 Hippo	7.3	AD 6 Occipital Ctx	30.8
Control (Path) 3 Hippo	2.0	Control 1 Occipital Ctx	3.1
AD 1 Temporal Ctx	36.9	Control 2 Occipital Ctx	38.2
AD 2 Temporal Ctx	62.4	Control 3 Occipital Ctx	33.4
AD 3 Temporal Ctx	16.0	Control 4 Occipital Ctx	2.8
AD 4 Temporal Ctx	26.4	Control (Path) 1 Occipital Ctx	93.3
AD 5 Inf Temporal Ctx	68.3	Control (Path) 2 Occipital Ctx	4.4
AD 5 Sup Temporal Ctx	44.1	Control (Path) 3 Occipital Ctx	5.1
AD 6 Inf Temporal Ctx	68.3	Control (Path) 4 Occipital Ctx	22.4
AD 6 Sup Temporal Ctx	64.6	Control 1 Parietal Ctx	7.6
Control 1 Temporal Ctx	6.2	Control 2 Parietal Ctx	48.3
Control 2 Temporal Ctx	62.9	Control 3 Parietal Ctx	41.5
Control 3 Temporal Ctx	45.4	Control (Path) 1 Parietal Ctx	84.7
Control 3 Temporal Ctx	7.1	Control (Path) 2 Parietal Ctx	31.2
Control (Path) 1 Temporal Ctx	100.0	Control (Path) 3 Parietal Ctx	1.0
Control (Path) 2 Temporal Ctx	57.8	Control (Path) 4 Parietal Ctx	67.8

Table ARC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3331, Run 215678710	Tissue Name	Rel. Exp.(%) Ag3331, Run 215678710
Adipose	0.4	Renal ca. TK-10	0.0
Melanoma* Hs688(A).T	0.0	Bladder	0.3
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	0.2

Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	0.0	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	0.2
Squamous cell carcinoma SCC-4	0.0	Colon ca.* (SW480 met) SW620	0.0
Testis Pool	100.0	Colon ca. HT29	0.0
Prostate ca.* (bone met) PC-3	0.0	Colon ca. HCT-116	0.0
Prostate Pool	0.1	Colon ca. CaCo-2	0.0
Placenta	0.2	Colon cancer tissue	0.2
Uterus Pool	0.1	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	0.0	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	0.0	Colon Pool	0.0
Ovarian ca. OVCAR-5	0.5	Small Intestine Pool	0.0
Ovarian ca. IGROV-1	0.0	Stomach Pool	0.0
Ovarian ca. OVCAR-8	0.0	Bone Marrow Pool	0.1
Ovary	0.0	Fetal Heart	0.0
Breast ca. MCF-7	0.0	Heart Pool	0.1
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	0.3
Breast ca. BT 549	0.0	Fetal Skeletal Muscle	0.2
Breast ca. T47D	0.2	Skeletal Muscle Pool	0.0
Breast ca. MDA-N	0.0	Spleen Pool	1.3
Breast Pool	0.0	Thymus Pool	0.6
Trachea	0.6	CNS cancer (glio/astro) U87-MG	0.0
Lung	0.0	CNS cancer (glio/astro) U-118-MG	0.0
Fetal Lung	0.5	CNS cancer (neuro;met) SK-N-AS	0.0
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	0.0	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	0.6	CNS cancer (glio) SNB-19	0.0
Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	0.0
Lung ca. A549	0.0	Brain (Amygdala) Pool	4.0
Lung ca. NCI-H526	1.2	Brain (cerebellum)	12.8
Lung ca. NCI-H23	0.0	Brain (fetal)	12.4
Lung ca. NCI-H460	0.0	Brain (Hippocampus) Pool	3.9
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	5.0
Lung ca. NCI-H522	0.1	Brain (Substantia nigra) Pool	4.2
Liver	0.0	Brain (Thalamus) Pool	6.9
Fetal Liver	0.1	Brain (whole)	6.7
Liver ca. HepG2	0.0	Spinal Cord Pool	0.2
Kidney Pool	0.1	Adrenal Gland	0.1
Fetal Kidney	0.3	Pituitary gland Pool	0.0
Renal ca. 786-0	0.0	Salivary Gland	0.0
Renal ca. A498	0.0	Thyroid (female)	0.5
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.0	Pancreas Pool	0.1

Table ARD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3331, Run 165084166	Tissue Name	Rel. Exp.(%) Ag3331, Run 165084166
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0

Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	9.3
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	9.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	0.0
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	6.7	Lung fibroblast TNF alpha + IL-1 beta	10.5
PBMC PHA-L	9.3	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	100.0	IBD Crohn's	10.4
Monocytes LPS	9.2	Colon	7.6

Macrophages rest	6.7	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag3331 This panel confirms the expression of this gene at low levels in the brains of an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3331 Expression of the CG57785-01 gene is highest in a sample derived from testis (CT = 28.6). Thus, the expression of this gene could be used to distinguish testis from the other samples in the panel. In addition, therapeutic modulation of the activity of this gene or its protein product, through the use of small molecule drugs, protein therapeutics or antibodies, might be beneficial in the treatment of fertility and hypogonadism.

This gene is also expressed at low to moderate levels throughout the CNS, including in amygdala, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

Panel 4D Summary: The CG57785-01 transcript is expressed at detectable levels only in resting monocytes (CT = 34.3). Thus, the expression of this gene could be used to distinguish resting monocytes from the other samples in the panel. In addition, the protein encoded by this transcript may be important in monocytic differentiation and activation. Therefore, regulating the expression of this transcript or the function of the protein it encodes may alter the types and levels of monocytic cells regulated by cytokine and chemokine production and T cell activation. Therapeutics designed with the protein encoded by this transcript could therefore be important for the treatment of asthma, emphysema, inflammatory bowel disease, arthritis and psoriasis.

AS. CG57748-01: N-acetylgalactosaminyltransferase

Expression of gene CG57748-01 was assessed using the primer-probe set Ag3325, described in Table ASA.

Table ASA. Probe Name Ag3325

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-tggcaccttctaagttaa-3'	22	1942	419
Probe	TET-5'-tttcaggtactcagatgtaccctg-3'-TAMRA	26	1969	420
Reverse	5'-cgcggtgtaataacgtttgaag-3'	22	2018	421

CNS_neurodegeneration_v1.0 Summary: Ag3325 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3325 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

5 **Panel 4D Summary:** Ag3325 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel due to a probable experimental failure (data not shown).

AT. CG57693-01: Novel Protein Kinase

10 Expression of gene CG57693-01 was assessed using the primer-probe set Ag3309, described in Table ATA. Results of the RTQ-PCR runs are shown in Tables ATB, ATC and ATD.

Table ATA. Probe Name Ag3309

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ttctacatggctcctgaagtct-3'	22	1540	422
Probe	TET-5'-actacacagccaaggcggacatcttt-3'-TAMRA	26	1571	423
Reverse	5'-tcttctatcattgccagatg-3'	22	1611	424

Table ATB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3309, Run 210143041	Tissue Name	Rel. Exp.(%) Ag3309, Run 210143041
AD 1 Hippo	9.5	Control (Path) 3 Temporal Ctx	3.7
AD 2 Hippo	21.2	Control (Path) 4 Temporal Ctx	26.2
AD 3 Hippo	4.6	AD 1 Occipital Ctx	19.5
AD 4 Hippo	3.0	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	100.0	AD 3 Occipital Ctx	5.4
AD 6 Hippo	44.4	AD 4 Occipital Ctx	12.2
Control 2 Hippo	18.9	AD 5 Occipital Ctx	16.4
Control 4 Hippo	7.7	AD 6 Occipital Ctx	40.6
Control (Path) 3 Hippo	3.9	Control 1 Occipital Ctx	3.5
AD 1 Temporal Ctx	13.1	Control 2 Occipital Ctx	63.3

AD 2 Temporal Ctx	21.9	Control 3 Occipital Ctx	17.2
AD 3 Temporal Ctx	6.4	Control 4 Occipital Ctx	4.2
AD 4 Temporal Ctx	17.6	Control (Path) 1 Occipital Ctx	72.2
AD 5 Inf Temporal Ctx	83.5	Control (Path) 2 Occipital Ctx	8.1
AD 5 Sup Temporal Ctx	31.0	Control (Path) 3 Occipital Ctx	2.7
AD 6 Inf Temporal Ctx	46.7	Control (Path) 4 Occipital Ctx	12.9
AD 6 Sup Temporal Ctx	43.8	Control 1 Parietal Ctx	5.4
Control 1 Temporal Ctx	6.3	Control 2 Parietal Ctx	39.2
Control 2 Temporal Ctx	32.5	Control 3 Parietal Ctx	11.0
Control 3 Temporal Ctx	13.3	Control (Path) 1 Parietal Ctx	54.7
Control 4 Temporal Ctx	5.0	Control (Path) 2 Parietal Ctx	15.5
Control (Path) 1 Temporal Ctx	46.0	Control (Path) 3 Parietal Ctx	2.6
Control (Path) 2 Temporal Ctx	28.5	Control (Path) 4 Parietal Ctx	37.1

Table ATC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3309, Run 215648362	Tissue Name	Rel. Exp.(%) Ag3309, Run 215648362
Adipose	8.1	Renal ca. TK-10	45.4
Melanoma* Hs688(A).T	19.6	Bladder	13.9
Melanoma* Hs688(B).T	20.9	Gastric ca. (liver met.) NCI-N87	73.2
Melanoma* M14	35.6	Gastric ca. KATO III	100.0
Melanoma* LOXIMVI	28.9	Colon ca. SW-948	8.4
Melanoma* SK-MEL-5	31.4	Colon ca. SW480	63.7
Squamous cell carcinoma SCC-4	28.9	Colon ca. * (SW480 met) SW620	52.9
Testis Pool	19.8	Colon ca. HT29	26.4
Prostate ca. * (bone met) PC-3	72.7	Colon ca. HCT-116	61.6
Prostate Pool	4.9	Colon ca. CaCo-2	47.3
Placenta	18.0	Colon cancer tissue	23.5
Uterus Pool	2.1	Colon ca. SW1116	8.8

Ovarian ca. OVCAR-3	24.1	Colon ca. Colo-205	18.6
Ovarian ca. SK-OV-3	40.6	Colon ca. SW-48	19.6
Ovarian ca. OVCAR-4	17.7	Colon Pool	10.2
Ovarian ca. OVCAR-5	43.5	Small Intestine Pool	11.8
Ovarian ca. IGROV-1	18.3	Stomach Pool	9.0
Ovarian ca. OVCAR-8	13.7	Bone Marrow Pool	5.9
Ovary	6.5	Fetal Heart	7.1
Breast ca. MCF-7	31.2	Heart Pool	4.7
Breast ca. MDA-MB-231	37.6	Lymph Node Pool	12.2
Breast ca. BT 549	36.6	Fetal Skeletal Muscle	3.8
Breast ca. T47D	68.3	Skeletal Muscle Pool	6.6
Breast ca. MDA-N	14.5	Spleen Pool	9.2
Breast Pool	9.6	Thymus Pool	13.6
Trachea	14.0	CNS cancer (glio/astro) U87-MG	16.7
Lung	2.3	CNS cancer (glio/astro) U-118-MG	62.9
Fetal Lung	21.8	CNS cancer (neuro;met) SK-N-AS	30.1
Lung ca. NCI-N417	4.9	CNS cancer (astro) SF-539	12.9
Lung ca. LX-1	52.5	CNS cancer (astro) SNB-75	50.3
Lung ca. NCI-H146	22.5	CNS cancer (glio) SNB-19	16.4
Lung ca. SHP-77	39.2	CNS cancer (glio) SF-295	23.2
Lung ca. A549	38.7	Brain (Amygdala) Pool	9.1
Lung ca. NCI-H526	17.1	Brain (cerebellum)	23.8
Lung ca. NCI-H23	39.2	Brain (fetal)	18.7
Lung ca. NCI-H460	24.5	Brain (Hippocampus) Pool	9.2
Lung ca. HOP-62	27.4	Cerebral Cortex Pool	11.7
Lung ca. NCI-H522	37.9	Brain (Substantia nigra) Pool	7.9
Liver	2.4	Brain (Thalamus) Pool	14.0
Fetal Liver	25.3	Brain (whole)	16.8
Liver ca. HepG2	49.7	Spinal Cord Pool	4.9
Kidney Pool	21.0	Adrenal Gland	24.1
Fetal Kidney	9.5	Pituitary gland Pool	3.7
Renal ca. 786-0	16.4	Salivary Gland	8.8
Renal ca. A498	6.0	Thyroid (female)	5.7
Renal ca. ACHN	16.7	Pancreatic ca. CAPAN2	37.4
Renal ca. UO-31	25.2	Pancreas Pool	14.8

Table ATD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3309, Run 164335487	Tissue Name	Rel. Exp.(%) Ag3309, Run 164335487
Secondary Th1 act	24.7	HUVEC IL-1beta	10.7
Secondary Th2 act	33.7	HUVEC IFN gamma	18.7
Secondary Tr1 act	31.9	HUVEC TNF alpha + IFN gamma	13.4
Secondary Th1 rest	5.8	HUVEC TNF alpha + IL4	16.3
Secondary Th2 rest	7.9	HUVEC IL-11	11.4
Secondary Tr1 rest	9.4	Lung Microvascular EC none	13.9
Primary Th1 act	28.3	Lung Microvascular EC TNFalpha + IL-1beta	15.7
Primary Th2 act	28.1	Microvascular Dermal EC none	19.3
Primary Tr1 act	37.9	Microsvascular Dermal EC TNFalpha + IL-1beta	16.3
Primary Th1 rest	49.0	Bronchial epithelium TNFalpha + IL1beta	36.3
Primary Th2 rest	26.8	Small airway epithelium none	9.5
Primary Tr1 rest	22.8	Small airway epithelium TNFalpha + IL-1beta	64.2
CD45RA CD4 lymphocyte act	14.9	Coronary artery SMC rest	14.9
CD45RO CD4 lymphocyte act	23.7	Coronary artery SMC TNFalpha + IL-1beta	8.1
CD8 lymphocyte act	17.3	Astrocytes rest	14.6
Secondary CD8 lymphocyte rest	21.8	Astrocytes TNFalpha + IL-1beta	9.0
Secondary CD8 lymphocyte act	15.7	KU-812 (Basophil) rest	17.8
CD4 lymphocyte none	5.5	KU-812 (Basophil) PMA/ionomycin	53.6
2ry Th1/Th2/Tr1_anti-CD95 CH11	12.2	CCD1106 (Keratinocytes) none	48.6
LAK cells rest	15.3	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	25.5
LAK cells IL-2	24.7	Liver cirrhosis	3.4
LAK cells IL-2+IL-12	28.5	Lupus kidney	2.3
LAK cells IL-2+IFN gamma	36.1	NCI-H292 none	21.6
LAK cells IL-2+ IL-18	23.0	NCI-H292 IL-4	31.4
LAK cells PMA/ionomycin	8.2	NCI-H292 IL-9	24.7
NK Cells IL-2 rest	20.3	NCI-H292 IL-13	15.2
Two Way MLR 3 day	18.6	NCI-H292 IFN gamma	18.2

Two Way MLR 5 day	17.9	HPAEC none	12.3
Two Way MLR 7 day	11.1	HPAEC TNF alpha + IL-1 beta	15.7
PBMC rest	10.0	Lung fibroblast none	10.1
PBMC PWM	77.4	Lung fibroblast TNF alpha + IL-1 beta	11.1
PBMC PHA-L	32.3	Lung fibroblast IL-4	24.5
Ramos (B cell) none	26.4	Lung fibroblast IL-9	18.7
Ramos (B cell) ionomycin	100.0	Lung fibroblast IL-13	17.6
B lymphocytes PWM	97.3	Lung fibroblast IFN gamma	26.4
B lymphocytes CD40L and IL-4	53.2	Dermal fibroblast CCD1070 rest	40.1
EOL-1 dbcAMP	15.1	Dermal fibroblast CCD1070 TNF alpha	59.9
EOL-1 dbcAMP PMA/ionomycin	27.5	Dermal fibroblast CCD1070 IL-1 beta	17.1
Dendritic cells none	9.3	Dermal fibroblast IFN gamma	9.5
Dendritic cells LPS	7.2	Dermal fibroblast IL-4	18.6
Dendritic cells anti-CD40	7.3	IBD Colitis 2	2.0
Monocytes rest	13.1	IBD Crohn's	2.0
Monocytes LPS	15.7	Colon	25.0
Macrophages rest	12.1	Lung	19.9
Macrophages LPS	9.9	Thymus	27.2
HUVEC none	20.4	Kidney	33.2
HUVEC starved	43.5		

CNS_neurodegeneration_v1.0 Summary: Ag3309 This panel confirms the expression of the CG57693-01 gene at moderate levels in the brains of an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3309 The CG57693-01 gene is expressed at high to moderate levels in the majority of samples on this panel, with highest expression detected in a gastric cancer cell line (CT = 26.7). This gene encodes a protein with homology to Ser/Thr protein kinases. In general, expression of this gene appears to be higher in cancer cell lines than in the corresponding normal tissues. This overexpression is particularly evident in lung, colon, prostate and gastric cancer cell lines. Therefore, therapeutic modulation of the activity of this gene and its protein product may be of benefit in the treatment

of lung, colon, prostate and gastric cancer. Furthermore, expression of this gene is significantly higher in fetal lung than in adult lung, suggesting that its expression may be used to distinguish fetal (CT = 28.9) from adult lung (CT = 32.1).

In addition, this gene is expressed at moderate levels throughout the CNS, including in amygdala, hippocampus, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

Among tissues with metabolic or endocrine function, this gene is expressed at moderate levels in pancreas, adipose, adrenal gland, thyroid, pituitary gland, heart, skeletal muscle and liver. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes. Interestingly, expression of this gene is higher in fetal liver (CT = 28.7) than in adult liver (CT = 32.1), suggesting that expression of this gene can be used to distinguish adult from fetal liver.

Panel 4D Summary: Ag3309 This transcript is highly expressed in the PMA and ionomycin treated basophil cell line KU-812 (CT=28.2) and to a lesser extent in untreated KU-812 cells (CT=29.8). Therefore, antibody or small molecule therapies designed with the protein encoded for by this gene could block or inhibit inflammation or tissue damage due to basophil activation in response to asthma, allergies, hypersensitivity reactions, psoriasis, and viral infections.

This gene is also moderately expressed in Ramos B cells (CT = 29.3) and the expression is highly stimulated by treatment with ionomycin and PWM (CTs=27). Expression of this transcript in B cells suggests that this gene may be involved in rheumatic disease including rheumatoid arthritis, lupus, osteoarthritis, and hyperproliferative B cell disorders.

In addition, treatment of small airway epithelium with TNFalpha + IL-1beta stimulated the expression of this transcript. Therefore, modulation of the expression or activity of the protein encoded by this transcript through the application of small molecule therapeutics may be useful in the treatment of asthma, COPD, and emphysema.

NOV54

Expression of NOV54/CG57707-01 was assessed using the primer-probe set Ag3312, described in Table AUA. Results of the RTQ-PCR runs are shown in Tables AUB, AUC and AUD.

Table AUA. Probe Name Ag3312

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gaccagcttgactatgaatgc-3'	22	624	425
Probe	TET-5'-tggtcatcagactttaccctaccagtcgg-3'-TAMRA	29	663	426
Reverse	5'-ggagtggaacgtatccactgaa-3'	22	693	427

5 **Table AUB.** CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3312, Run 210143316	Tissue Name	Rel. Exp.(%) Ag3312, Run 210143316
AD 1 Hippo	2.1	Control (Path) 3 Temporal Ctx	1.2
AD 2 Hippo	7.7	Control (Path) 4 Temporal Ctx	12.5
AD 3 Hippo	0.9	AD 1 Occipital Ctx	10.9
AD 4 Hippo	2.8	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	100.0	AD 3 Occipital Ctx	2.2
AD 6 Hippo	10.3	AD 4 Occipital Ctx	6.6
Control 2 Hippo	17.1	AD 5 Occipital Ctx	54.7
Control 4 Hippo	3.1	AD 6 Occipital Ctx	12.9
Control (Path) 3 Hippo	2.5	Control 1 Occipital Ctx	5.2
AD 1 Temporal Ctx	5.1	Control 2 Occipital Ctx	84.7
AD 2 Temporal Ctx	6.7	Control 3 Occipital Ctx	6.9
AD 3 Temporal Ctx	1.2	Control 4 Occipital Ctx	0.9
AD 4 Temporal Ctx	5.3	Control (Path) 1 Occipital Ctx	66.0
AD 5 Inf Temporal Ctx	52.9	Control (Path) 2 Occipital Ctx	4.1
AD 5 Sup Temporal Ctx	14.0	Control (Path) 3 Occipital Ctx	3.7
AD 6 Inf Temporal Ctx	7.4	Control (Path) 4 Occipital Ctx	13.6
AD 6 Sup Temporal Ctx	8.1	Control 1 Parietal Ctx	3.0
Control 1 Temporal Ctx	5.6	Control 2 Parietal Ctx	7.9
Control 2 Temporal Ctx	27.0	Control 3 Parietal Ctx	16.8
Control 3 Temporal Ctx	8.6	Control (Path) 1 Parietal Ctx	79.0
Control 3 Temporal Ctx	1.4	Control (Path) 2 Parietal Ctx	11.8
Control (Path) 1 Temporal Ctx	25.7	Control (Path) 3 Parietal Ctx	4.6
Control (Path) 2 Temporal Ctx	21.8	Control (Path) 4 Parietal Ctx	34.9

Table AUC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3312, Run 215648085	Tissue Name	Rel. Exp.(%) Ag3312, Run 215648085
Adipose	11.8	Renal ca. TK-10	38.2
Melanoma* Hs688(A).T	0.0	Bladder	8.5
Melanoma* Hs688(B).T	0.1	Gastric ca. (liver met.) NCI-N87	2.8

Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMV1	0.3	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	3.6	Colon ca. SW480	0.2
Squamous cell carcinoma SCC-4	0.5	Colon ca.* (SW480 met) SW620	0.4
Testis Pool	9.0	Colon ca. HT29	0.0
Prostate ca.* (bone met) PC-3	0.0	Colon ca. HCT-116	0.0
Prostate Pool	2.0	Colon ca. CaCo-2	11.6
Placenta	9.5	Colon cancer tissue	21.9
Uterus Pool	19.2	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	29.3	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	8.4	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	4.3	Colon Pool	59.9
Ovarian ca. OVCAR-5	5.0	Small Intestine Pool	26.6
Ovarian ca. IGROV-1	34.6	Stomach Pool	35.6
Ovarian ca. OVCAR-8	2.2	Bone Marrow Pool	20.7
Ovary	8.9	Fetal Heart	18.6
Breast ca. MCF-7	0.5	Heart Pool	20.7
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	55.1
Breast ca. BT 549	18.4	Fetal Skeletal Muscle	8.2
Breast ca. T47D	4.3	Skeletal Muscle Pool	4.6
Breast ca. MDA-N	0.0	Spleen Pool	2.6
Breast Pool	36.9	Thymus Pool	16.6
Trachea	7.2	CNS cancer (glio/astro) U87-MG	2.4
Lung	10.5	CNS cancer (glio/astro) U-118-MG	3.6
Fetal Lung	36.6	CNS cancer (neuro;met) SK-N-AS	6.9
Lung ca. NCI-N417	11.0	CNS cancer (astro) SF-539	0.9
Lung ca. LX-1	0.0	CNS cancer (astro) SNB-75	6.0
Lung ca. NCI-H146	48.6	CNS cancer (glio) SNB-19	41.5
Lung ca. SHP-77	2.1	CNS cancer (glio) SF-295	1.0
Lung ca. A549	0.0	Brain (Amygdala) Pool	30.1
Lung ca. NCI-H526	3.2	Brain (cerebellum)	100.0
Lung ca. NCI-H23	10.4	Brain (fetal)	33.2
Lung ca. NCI-H460	2.0	Brain (Hippocampus) Pool	31.9
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	51.1
Lung ca. NCI-H522	3.1	Brain (Substantia nigra) Pool	50.7
Liver	0.7	Brain (Thalamus) Pool	43.2
Fetal Liver	3.0	Brain (whole)	55.1
Liver ca. HepG2	0.0	Spinal Cord Pool	23.3
Kidney Pool	67.4	Adrenal Gland	8.8
Fetal Kidney	83.5	Pituitary gland Pool	0.0
Renal ca. 786-0	0.0	Salivary Gland	1.8
Renal ca. A498	2.0	Thyroid (female)	5.6
Renal ca. ACHN	0.2	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.0	Pancreas Pool	35.6

Table AUD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3312, Run 164682846	Tissue Name	Rel. Exp.(%) Ag3312, Run 164682846
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.9

Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.4
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	1.7
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.6
LAK cells IL-2	0.0	Liver cirrhosis	2.2
LAK cells IL-2+IL-12	2.2	Lupus kidney	3.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	13.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	12.2
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	24.7
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	8.9
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	5.4
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.8
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.8
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.8
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.7
B lymphocytes PWM	1.3	Lung fibroblast IFN gamma	3.0
B lymphocytes CD40L and IL-4	0.9	Dermal fibroblast CCD1070 rest	2.2
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	2.8
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	8.1
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	11.0
Monocytes rest	0.0	IBD Crohn's	16.4
Monocytes LPS	0.0	Colon	100.0

Macrophages rest	8.2	Lung	69.3
Macrophages LPS	1.0	Thymus	47.3
HUVEC none	0.0	Kidney	23.7
HUVEC starved	0.0		

CNS_neurodegeneration_v1.0 Summary: Ag3312 This panel confirms the expression of CG57707-01 gene at low to moderate levels in the brains of an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3312 Expression of the CG57707-01 gene is highest in the cerebellum (CT = 27.6). This gene is also expressed at moderate levels in all other regions of the central nervous system examined, including amygdala, hippocampus, substantia nigra, thalamus, cerebral cortex and spinal cord. The CG57707-01 gene encodes a protein with homology to the leucine-rich glioma-activated gene (LGI1). Recently, mutations in the LGI1 gene have been shown to cause autosomal-dominant partial epilepsy with auditory features (ref. 1). Based upon its homology to the LGI1 gene and significant expression in the brain, the CG57707-01 gene may also play a role in epilepsy or other central nervous system disorders such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, schizophrenia and depression.

Strikingly, expression of this gene is primarily associated with the normal tissues on this panel. CG57707-01 gene expression appears to be down-regulated in pancreatic, colon, gastric, renal, lung, breast and prostate cancer cell lines as well as in most astrocytoma and glioma cell lines when compared to their respective normal tissues. This observation is consistent with what is known about the LGI1 gene, which was originally identified on the basis of its downregulation in malignant brain tumors (Ref.1, 2). Therefore, therapeutic modulation of the activity of the CG57707-01 gene or its protein product, using small molecule drugs, antibodies or protein therapeutics, may be of benefit in the treatment of pancreatic, colon, gastric, renal, lung, breast, prostate, and CNS cancers.

Among tissues with metabolic or endocrine function, this gene is expressed at moderate levels in pancreas, adipose, adrenal gland, thyroid, skeletal muscle and heart. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes.

References:

1. Kalachikov S, Evgrafov O, Ross B, Winawer M, Barker Cummings C, Boneschi FM, Choi C, Morozov P, Das K, Teplitskaya E, Yu A, Cayanis E, Penchaszadeh G, Kottmann AH, Pedley TA, Hauser WA, Ottman R, Gilliam TC. Mutations in LGI1 cause autosomal-dominant partial epilepsy with auditory features. *Nat Genet* 2002 Jan 28; [epub ahead of print]

The epilepsies are a common, clinically heterogeneous group of disorders defined by recurrent unprovoked seizures. Here we describe identification of the causative gene in autosomal-dominant partial epilepsy with auditory features (ADPEAF, MIM 600512), a rare form of idiopathic lateral temporal lobe epilepsy characterized by partial seizures with auditory disturbances. We constructed a complete, 4.2-Mb physical map across the genetically implicated disease gene region, identified 28 putative genes (Fig. 1) and resequenced all or part of 21 genes before identifying presumptive mutations in one copy of the leucine-rich, glioma-inactivated 1 gene (LGI1) in each of five families with ADPEAF. Previous studies have indicated that loss of both copies of LGI1 promotes glial tumor progression. We show that the expression pattern of mouse *Lgi1* is predominantly neuronal and is consistent with the anatomic regions involved in temporal lobe epilepsy. Discovery of LGI1 as a cause of ADPEAF suggests new avenues for research on pathogenic mechanisms of idiopathic epilepsies.

PMID: 11810107

2. Chernova OB, Somerville RP, Cowell JK. A novel gene, LGI1, from 10q24 is rearranged and downregulated in malignant brain tumors. *Oncogene* 1998 Dec 3;17(22):2873-81

Loss of heterozygosity for 10q23-26 is seen in over 80% of glioblastoma multiforme tumors. We have used a positional cloning strategy to isolate a novel gene, LGI1 (Leucine rich gene-Glioma Inactivated), which is rearranged as a result of the t(10;19)(q24;q13) balanced translocation in the T98G glioblastoma cell line lacking any normal chromosome 10. Rearrangement of the LGI1 gene was also detected in the A172 glioblastoma cell line and several glioblastoma tumors. These rearrangements lead to a complete absence of LGI1 expression in glioblastoma cells. The LGI1 gene encodes a protein with a calculated molecular mass of 60 kD and contains 3.5 leucine-rich repeats (LRR) with conserved flanking sequences. In the LRR domain, LGI1 has the highest homology with a number of transmembrane and extracellular proteins which function as receptors and adhesion proteins. LGI1 is predominantly expressed in neural tissues, especially in brain; its expression is reduced in low grade brain tumors and it is significantly reduced or absent in malignant gliomas. Its

localization to the 10q24 region, and rearrangements or inactivation in malignant brain tumors, suggest that LGI1 is a candidate tumor suppressor gene involved in progression of glial tumors.

PMID: 9879993

5 **Panel 4D Summary:** Ag3312 The CG57707-01 gene is moderately expressed in samples derived from normal colon (CT=29.9), lung (CT=30.4), thymus (CT=30.9) and kidney (CT=31.9). Thus, the expression of this gene could be used to distinguish these tissues from the other samples in this panel. Expression of this gene in normal tissues is consistent with what is observed in General_screening_panel_v1.4.

10 Furthermore, expression of this gene is decreased in colon samples from patients with IBD colitis (CT=33) and Crohn's disease (CT=32.5) relative to normal colon. Therefore, therapeutic modulation of the activity of the protein encoded by this gene may be useful in the treatment of inflammatory bowel disease.

NOV55

15 Expression of NOV55/CG57306-01 was assessed using the primer-probe set Ag3157, described in Table AVA. Results of the RTQ-PCR runs are shown in Tables AVB, and AVC.

Table AVA. Probe Name Ag3157

Primers	Sequences	Length	Start Position
Forward	5'-tgatcacagtcacagacattg-3'	22	1766
Probe	TET-5'-ccttcttctcccttctctcttctt-3'-TAMRA	26	1788
Reverse	5'-ggctgggtctttacacacttgag-3'	22	1838

Table AVB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag3157, Run 167994581	Tissue Name	Rel. Exp.(%) Ag3157, Run 167994581
Liver adenocarcinoma	0.0	Kidney (fetal)	48.6
Pancreas	0.2	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	1.1	Renal ca. A498	0.2
Adrenal gland	0.0	Renal ca. RXF 393	0.5
Thyroid	0.6	Renal ca. ACHN	0.0
Salivary gland	1.2	Renal ca. UO-31	0.2
Pituitary gland	0.2	Renal ca. TK-10	0.0
Brain (fetal)	2.9	Liver	0.2
Brain (whole)	5.5	Liver (fetal)	0.2

Brain (amygdala)	2.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	2.0	Lung	0.8
Brain (hippocampus)	1.5	Lung (fetal)	0.0
Brain (substantia nigra)	3.5	Lung ca. (small cell) LX-1	0.8
Brain (thalamus)	1.6	Lung ca. (small cell) NCI- H69	0.0
Cerebral Cortex	1.6	Lung ca. (s.cell var.) SHP- 77	0.9
Spinal cord	1.7	Lung ca. (large cell) NCI- H460	0.0
glio/astro U87-MG	0.5	Lung ca. (non-sm. cell) A549	1.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI- H23	1.4
astrocytoma SW1783	0.2	Lung ca. (non-s.cell) HOP- 62	0.2
neuro*; met SK-N-AS	0.5	Lung ca. (non-s.cl) NCI- H522	1.2
astrocytoma SF-539	0.5	Lung ca. (squam.) SW 900	0.1
astrocytoma SNB-75	0.4	Lung ca. (squam.) NCI- H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.3	Breast ca.* (pl.ef) MCF-7	1.0
glioma SF-295	0.2	Breast ca.* (pl.ef) MDA- MB-231	0.2
Heart (fetal)	0.4	Breast ca.* (pl.ef) T47D	1.8
Heart	0.2	Breast ca. BT-549	0.8
Skeletal muscle (fetal)	0.6	Breast ca. MDA-N	0.4
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.2	Ovarian ca. OVCAR-3	0.4
Thymus	0.2	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	2.7
Lymph node	0.0	Ovarian ca. OVCAR-8	0.2
Colorectal	0.5	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK- OV-3	0.9
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.2	Placenta	0.0
Colon ca.* SW620(SW480	1.6	Prostate	0.5

met)			
Colon ca. HT29	0.2	Prostate ca.* (bone met)PC-3	0.9
Colon ca. HCT-116	1.3	Testis	1.3
Colon ca. CaCo-2	0.5	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.2
Colon ca. HCC-2998	2.6	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.3	Melanoma M14	0.3
Bladder	0.5	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	1.5
Kidney	100.0	Adipose	0.4

Table AVC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3157, Run 164529941	Tissue Name	Rel. Exp.(%) Ag3157, Run 164529941
Secondary Th1 act	0.2	HUVEC IL-1beta	0.0
Secondary Th2 act	0.3	HUVEC IFN gamma	0.1
Secondary Tr1 act	1.1	HUVEC TNF alpha + IFN gamma	0.4
Secondary Th1 rest	0.7	HUVEC TNF alpha + IL4	0.1
Secondary Th2 rest	0.4	HUVEC IL-11	0.4
Secondary Tr1 rest	0.6	Lung Microvascular EC none	0.2
Primary Th1 act	0.4	Lung Microvascular EC TNFalpha + IL-1beta	0.3
Primary Th2 act	0.2	Microvascular Dermal EC none	0.1
Primary Tr1 act	0.8	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	1.1	Bronchial epithelium TNFalpha + IL1beta	0.3
Primary Th2 rest	1.1	Small airway epithelium none	0.4
Primary Tr1 rest	0.2	Small airway epithelium TNFalpha + IL-1beta	0.2
CD45RA CD4 lymphocyte act	0.3	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	0.4	Coronary artery SMC TNFalpha + IL-1beta	0.1
CD8 lymphocyte act	0.0	Astrocytes rest	0.1
Secondary CD8 lymphocyte	0.2	Astrocytes TNFalpha + IL-1beta	0.2

rest			
Secondary CD8 lymphocyte act	0.3	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.2	KU-812 (Basophil) PMA/ionomycin	0.5
2ry Th1/Th2/Tr1 _anti-CD95 CH11	1.4	CCD1106 (Keratinocytes) none	0.1
LAK cells rest	0.1	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.2
LAK cells IL-2	0.9	Liver cirrhosis	1.0
LAK cells IL-2+IL-12	0.7	Lupus kidney	4.4
LAK cells IL-2+IFN gamma	0.4	NCI-H292 none	0.7
LAK cells IL-2+ IL-18	1.3	NCI-H292 IL-4	0.5
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	1.2
NK Cells IL-2 rest	0.3	NCI-H292 IL-13	0.1
Two Way MLR 3 day	0.8	NCI-H292 IFN gamma	0.2
Two Way MLR 5 day	0.1	HPAEC none	0.2
Two Way MLR 7 day	0.3	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	1.7	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.3	Lung fibroblast IL-4	0.3
Ramos (B cell) none	0.9	Lung fibroblast IL-9	0.1
Ramos (B cell) ionomycin	5.4	Lung fibroblast IL-13	0.2
B lymphocytes PWM	1.1	Lung fibroblast IFN gamma	0.1
B lymphocytes CD40L and IL-4	2.2	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	1.3
EOL-1 dbcAMP PMA/ionomycin	0.5	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.1
Dendritic cells LPS	0.2	Dermal fibroblast IL-4	0.2
Dendritic cells anti-CD40	0.1	IBD Colitis 2	0.0
Monocytes rest	0.0	IBD Crohn's	0.0
Monocytes LPS	0.7	Colon	0.6
Macrophages rest	0.1	Lung	1.1
Macrophages LPS	0.0	Thymus	100.0
HUVEC none	0.1	Kidney	0.3

HUVEC starved	1.0		
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Panel 1.3D Summary: Ag3157 Expression of the CG57306-01 gene is highest in samples derived from normal kidney (CT = 29.7) and fetal kidney (CT=30.8). Thus, the expression of this gene could be used to distinguish kidney from the other samples in the panel.

5 The CG57306-01 gene encodes a variant of anion exchanger AE4, which is expressed primarily in the kidney and is predicted to play a role in sodium bicarbonate exchange (ref. 1). Mutations in sodium bicarbonate transporters have been shown to be associated with renal tubular acidosis (RTA) (ref. 2-3). Thus, therapies designed with the protein encoded for by this gene may potentially play a role in the identification and treatment of RTA or other kidney
10 related diseases.

This transcript is also expressed at low levels in samples derived from brain, including whole adult brain (CT=33.9) and substantia nigra (CT=34.5). Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

15 References:

1. Parker MD, Ourmozdi EP, Tanner MJ. Human BTR1, a new bicarbonate transporter superfamily member and human AE4 from kidney. Biochem Biophys Res Commun 2001 Apr 20;282(5):1103-9

We report the cloning, characterization, and chromosomal localization of two novel
20 human members of the bicarbonate transporter superfamily, BTR1 (Bicarbonate Transporter Related protein-1) and AE4 (Anion Exchange protein 4). BTR1 is a novel mammalian protein. The BTR1 gene maps to chromosome 20p12 and encodes a 100 kDa protein predominantly expressed in the kidney, salivary glands, testis, thyroid glands, and trachea. The AE4 gene maps to chromosome 5q23-31 and encodes a 104 kDa protein expressed mainly in the kidney.
25 Human AE4 shares 84% identity with the recently reported rabbit AE4, a sodium independent, Cl(-)/HCO(-)(3) exchanger located on the apical membrane of beta-intercalated kidney cells. Copyright 2001 Academic Press.

PMID: 11302728

2. Soleimani M, Burnham CE. Physiologic and molecular aspects of the Na⁺:HCO₃⁻
30 cotransporter in health and disease processes. Kidney Int 2000 Feb;57(2):371-84

Approximately 80% of the filtered load of HCO_3^- is reabsorbed in the proximal tubule via a process of active acid secretion by the luminal membrane. The major mechanism for the transport of HCO_3^- across the basolateral membrane is via the electrogenic $\text{Na}^+:\text{HCO}_3^-$ cotransporter (NBC). Recent molecular cloning experiments have identified the existence of three NBC isoforms (NBC-1, NBC-2, and NBC-3).¹ Functional and molecular studies indicate the presence of all three NBC isoforms in the kidney. All are presumed to mediate the cotransport of Na^+ and HCO_3^- under normal conditions and may be functionally altered in certain pathophysiologic states. Specifically, NBC-1 may be up regulated in metabolic acidosis and potassium depletion and in response to glucocorticoid excess and may be down regulated in response to HCO_3^- loading or alkalosis. Recent studies provide molecular evidence indicating the expression of NBC-1 in pancreatic duct cells. NBC is activated by cystic fibrosis transmembrane conductance regulator (CFTR) and plays an important role in HCO_3^- secretion in the agonist-stimulated state in pancreatic duct cells. The purpose of this review is to summarize recent functional and molecular studies on the regulation of NBCs in physiologic and pathophysiologic states. Possible signals responsible for the regulation of NBCs in these conditions are examined. Furthermore, the possible role of this transporter in acid-base disorders (such as proximal renal tubular acidosis) is discussed.

PMID: 10652014

3. Rodriguez-Soriano J., 2000, New insights into the pathogenesis of renal tubular acidosis--from functional to molecular studies. *Pediatr Nephrol* Oct;14(12):1121-36.

The diagnosis and classification of renal tubular acidosis (RTA) have traditionally been made on the basis of functional studies. On these grounds, RTA has been separated into three main categories: (1) proximal RTA, or type 2; (2) distal RTA, or type 1; and (3) hyperkalemic RTA, or type 4. In recent years significant advances have been made in our understanding of the subcellular mechanisms involved in renal bicarbonate (HCO_3^-) and H^+ transport. Application of molecular biology techniques has also opened a completely new perspective to the understanding of the pathophysiology of inherited cases of RTA. Mutations in the gene *SLC4A4*, encoding $\text{Na}^+:\text{HCO}_3^-$ cotransporter (NBC-1), have been found in proximal RTA with ocular abnormalities; in the gene *SLC4A1*, encoding $\text{Cl}^-:\text{HCO}_3^-$ exchanger (AE1), in autosomal dominant distal RTA; in the gene *ATP6B1*, encoding B1 subunit of $\text{H}^+:\text{ATPase}$, in autosomal recessive distal RTA with sensorineural deafness; and in the gene *CA2*, encoding carbonic anhydrase II, in autosomal recessive osteopetrosis. Syndromes of aldosterone resistance have been also characterized molecularly and mutations in the gene *MLR*, encoding mineralocorticoid receptor, and in the genes *SNCC1A*, *SNCC1B*, and *SCNN1G*, encoding

subunits of the epithelial Na⁺ channel, have been found in dominant and recessive forms of pseudohypoaldosteronism type 1, respectively. It can be concluded that, although functional studies are still necessary, a new molecular era in the understanding of disorders of renal acidification has arrived.

5 PMID: 11045400

Panel 4D Summary: Ag3157 Expression of the CG57306-01 gene is highest in thymus (CT = 27.9). Therefore, expression of this gene can be used to distinguish thymus from the other samples on this panel. The putative anion exchanger encoded for by this gene could therefore play an important role in T cell development. Furthermore, small molecule
10 drugs or antibody therapeutics designed against the protein encoded for by this gene could be utilized to modulate immune function (T cell development) and be important for organ transplant, AIDS treatment or post chemotherapy immune reconstitution.

Panel 5 Islet Summary: Ag3157 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

15 **NOV56**

Expression of NOV56/CG57348-01 was assessed using the primer-probe set Ag3763, described in Table AWA. Results of the RTQ-PCR runs are shown in Tables AWB, AWC and AWD.

Table AWA. Probe Name Ag3763

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gatggggagagcgtattacc-3'	21	274	428
Probe	TET-5'-tcaagatctattcctacatgagccga-3'-TAMRA	28	301	429
Reverse	5'-aaacgcattccagagcattt-3'	20	331	430

20 Table AWB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3763, Run 211175130	Tissue Name	Rel. Exp.(%) Ag3763, Run 211175130
AD 1 Hippo	19.8	Control (Path) 3 Temporal Ctx	17.7
AD 2 Hippo	46.7	Control (Path) 4 Temporal Ctx	59.9
AD 3 Hippo	19.6	AD 1 Occipital Ctx	27.9
AD 4 Hippo	13.2	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	86.5	AD 3 Occipital Ctx	20.7
AD 6 Hippo	92.0	AD 4 Occipital Ctx	20.9
Control 2 Hippo	46.7	AD 5 Occipital Ctx	39.8
Control 4 Hippo	25.2	AD 6 Occipital Ctx	44.8
Control (Path) 3 Hippo	12.0	Control 1 Occipital Ctx	15.4
AD 1 Temporal Ctx	45.7	Control 2 Occipital Ctx	49.0

AD 2 Temporal Ctx	47.3	Control 3 Occipital Ctx	27.7
AD 3 Temporal Ctx	12.2	Control 4 Occipital Ctx	14.5
AD 4 Temporal Ctx	24.3	Control (Path) 1 Occipital Ctx	96.6
AD 5 Inf Temporal Ctx	100.0	Control (Path) 2 Occipital Ctx	28.9
AD 5 Sup Temporal Ctx	87.1	Control (Path) 3 Occipital Ctx	5.9
AD 6 Inf Temporal Ctx	61.1	Control (Path) 4 Occipital Ctx	35.1
AD 6 Sup Temporal Ctx	88.9	Control 1 Parietal Ctx	18.0
Control 1 Temporal Ctx	12.5	Control 2 Parietal Ctx	66.0
Control 2 Temporal Ctx	48.6	Control 3 Parietal Ctx	34.9
Control 3 Temporal Ctx	30.6	Control (Path) 1 Parietal Ctx	77.9
Control 4 Temporal Ctx	13.2	Control (Path) 2 Parietal Ctx	45.1
Control (Path) 1 Temporal Ctx	85.3	Control (Path) 3 Parietal Ctx	6.6
Control (Path) 2 Temporal Ctx	65.1	Control (Path) 4 Parietal Ctx	52.5

Table AWC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3763, Run 216557719	Tissue Name	Rel. Exp.(%) Ag3763, Run 216557719
Adipose	7.7	Renal ca. TK-10	24.8
Melanoma* Hs688(A).T	31.4	Bladder	17.6
Melanoma* Hs688(B).T	27.7	Gastric ca. (liver met.) NCI-N87	30.4
Melanoma* M14	30.8	Gastric ca. KATO III	42.0
Melanoma* LOXIMVI	29.1	Colon ca. SW-948	7.7
Melanoma* SK-MEL-5	19.2	Colon ca. SW480	40.6
Squamous cell carcinoma SCC-4	16.4	Colon ca.* (SW480 met) SW620	54.3
Testis Pool	6.4	Colon ca. HT29	18.9
Prostate ca.* (bone met) PC-3	52.9	Colon ca. HCT-116	58.2
Prostate Pool	23.8	Colon ca. CaCo-2	21.6
Placenta	9.3	Colon cancer tissue	21.8
Uterus Pool	7.9	Colon ca. SW1116	11.2
Ovarian ca. OVCAR-3	19.3	Colon ca. Colo-205	10.8
Ovarian ca. SK-OV-3	35.4	Colon ca. SW-48	11.2
Ovarian ca. OVCAR-4	13.7	Colon Pool	8.8
Ovarian ca. OVCAR-5	35.8	Small Intestine Pool	16.0
Ovarian ca. IGROV-1	31.9	Stomach Pool	11.0
Ovarian ca. OVCAR-8	52.1	Bone Marrow Pool	6.2
Ovary	4.5	Fetal Heart	6.0
Breast ca. MCF-7	37.9	Heart Pool	4.6
Breast ca. MDA-MB-231	36.9	Lymph Node Pool	14.1
Breast ca. BT 549	44.1	Fetal Skeletal Muscle	5.5
Breast ca. T47D	100.0	Skeletal Muscle Pool	12.2
Breast ca. MDA-N	12.2	Spleen Pool	12.3
Breast Pool	8.7	Thymus Pool	14.4
Trachea	16.3	CNS cancer (glio/astro) U87-MG	25.0
Lung	7.6	CNS cancer (glio/astro) U-	52.9

		118-MG	
Fetal Lung	15.0	CNS cancer (neuro;met) SK-N-AS	42.9
Lung ca. NCI-N417	14.8	CNS cancer (astro) SF-539	20.9
Lung ca. LX-1	47.3	CNS cancer (astro) SNB-75	18.9
Lung ca. NCI-H146	12.0	CNS cancer (glio) SNB-19	32.1
Lung ca. SHP-77	47.0	CNS cancer (glio) SF-295	63.3
Lung ca. A549	23.8	Brain (Amygdala) Pool	7.5
Lung ca. NCI-H526	17.1	Brain (cerebellum)	10.1
Lung ca. NCI-H23	64.6	Brain (fetal)	12.6
Lung ca. NCI-H460	26.2	Brain (Hippocampus) Pool	8.7
Lung ca. HOP-62	8.8	Cerebral Cortex Pool	11.5
Lung ca. NCI-H522	42.9	Brain (Substantia nigra) Pool	10.8
Liver	0.6	Brain (Thalamus) Pool	14.5
Fetal Liver	18.6	Brain (whole)	13.3
Liver ca. HepG2	10.1	Spinal Cord Pool	13.3
Kidney Pool	12.2	Adrenal Gland	9.9
Fetal Kidney	4.8	Pituitary gland Pool	3.5
Renal ca. 786-0	18.2	Salivary Gland	14.4
Renal ca. A498	10.4	Thyroid (female)	11.3
Renal ca. ACHN	17.1	Pancreatic ca. CAPAN2	17.7
Renal ca. UO-31	20.3	Pancreas Pool	21.5

Table AWD. Panel 4.1D

Tissue Name	Rel. Exp.(%) Ag3763, Run 170069604	Tissue Name	Rel. Exp.(%) Ag3763, Run 170069604
Secondary Th1 act	72.7	HUVEC IL-1beta	56.3
Secondary Th2 act	73.2	HUVEC IFN gamma	45.1
Secondary Tr1 act	58.2	HUVEC TNF alpha + IFN gamma	25.3
Secondary Th1 rest	8.7	HUVEC TNF alpha + IL4	37.4
Secondary Th2 rest	28.1	HUVEC IL-11	26.4
Secondary Tr1 rest	14.7	Lung Microvascular EC none	48.0
Primary Th1 act	52.1	Lung Microvascular EC TNFalpha + IL-1beta	27.2
Primary Th2 act	52.1	Microvascular Dermal EC none	48.3
Primary Tr1 act	52.5	Microvascular Dermal EC TNFalpha + IL-1beta	26.8
Primary Th1 rest	28.1	Bronchial epithelium TNFalpha + IL1beta	24.5
Primary Th2 rest	17.9	Small airway epithelium none	17.3
Primary Tr1 rest	36.9	Small airway epithelium TNFalpha + IL-1beta	27.9
CD45RA CD4 lymphocyte act	43.5	Coronary artery SMC rest	26.8
CD45RO CD4 lymphocyte act	43.2	Coronary artery SMC TNFalpha + IL-1beta	15.9
CD8 lymphocyte act	48.0	Astrocytes rest	29.9
Secondary CD8 lymphocyte rest	37.9	Astrocytes TNFalpha + IL-1beta	23.5
Secondary CD8 lymphocyte act	32.5	KU-812 (Basophil) rest	46.7
CD4 lymphocyte none	11.5	KU-812 (Basophil) PMA/ionomycin	60.3
2ry Th1/Th2/Tr1_anti-CD95 CH11	23.8	CCD1106 (Keratinocytes) none	34.9
LAK cells rest	29.7	CCD1106 (Keratinocytes)	29.5

In addition, this gene is expressed at low levels in all regions of the central nervous system examined, including in amygdala, hippocampus, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

This gene is also expressed at low levels in a number of tissues with metabolic or endocrine function, including adipose, pancreas, adrenal gland, thyroid, gastrointestinal tract, skeletal muscle, heart and liver. Therefore, therapeutic modulation of the activity of this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes. Interestingly, this gene is expressed at higher levels in fetal liver (CT = 32.2) when compared to adult liver (CT = 37.2), suggesting that expression of this gene can be used to distinguish fetal from adult liver and may be of benefit in the treatment of liver degeneration.

Panel 4.1D Summary: Ag3763 This gene is expressed at low to moderate levels in a wide range of cell types of significance to the immune response in health and disease. These cells include T-cells, B-cells, endothelial cells, macrophages, monocytes, dendritic cells, basophils, eosinophils and peripheral blood mononuclear cells, as well as epithelial and fibroblast cell types from lung and skin, and normal tissues represented by colon, lung, thymus and kidney. This ubiquitous pattern of expression suggests that this gene product may be involved in homeostatic processes for these and other cell types and tissues.

This pattern is in agreement with the expression profile in General_screening_panel_v1.4 and also suggests a role for the gene product in cell survival and proliferation.

Therefore, therapeutic modulation of the activity of this gene or its protein product may lead to the alteration of functions associated with these cell types and lead to improvement of the symptoms of patients suffering from autoimmune and inflammatory diseases such as asthma, allergies, inflammatory bowel disease, lupus erythematosus, psoriasis, rheumatoid arthritis, and osteoarthritis.

NOV60

Expression of gene NOV60/CG57574-01 was assessed using the primer-probe set Ag3289, described in Table AXA.

Table AXA. Probe Name Ag3289

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-accagcctgtcaactactcctt-3'	22	419	431
Probe	TET-5'-ccactccactacttgggtgaaccagg-3'-TAMRA	26	453	432
Reverse	5'-ggaaattgacactctgggtcaaa-3'	22	484	433

CNS_neurodegeneration_v1.0 Summary: Ag3289 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3289 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown). The amp plot indicates that there were experimental difficulties with this run.

Panel 4D Summary: Ag3289 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV61

Expression of NOV61/CG57505-01 was assessed using the primer-probe set Ag3259, described in Table AYA. Results of the RTQ-PCR runs are shown in Tables AYB, AYC and AYD.

Table AYA. Probe Name Ag3259

Primers	Sequences	Length	Start Position	SEQ ID NO:
Forward	5'-catcgagaccagagtaaagc-3'	21	604	434
Probe	TET-5'-catgacaatgctcaccattgaacagt-3'-TAMRA	26	625	435
Reverse	5'-tttcattttctgaatggcaaac-3'	22	667	436

Table AYB. CNS_neurodegeneration v1.0

Tissue Name	Rel. Exp.(%) Ag3259, Run 209990878	Tissue Name	Rel. Exp.(%) Ag3259, Run 209990878
AD 1 Hippo	7.1	Control (Path) 3 Temporal Ctx	3.5
AD 2 Hippo	14.9	Control (Path) 4 Temporal Ctx	16.8
AD 3 Hippo	5.8	AD 1 Occipital Ctx	8.3
AD 4 Hippo	4.3	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	100.0	AD 3 Occipital Ctx	6.6
AD 6 Hippo	6.1	AD 4 Occipital Ctx	9.7
Control 2 Hippo	11.9	AD 5 Occipital Ctx	6.8
Control 4 Hippo	7.5	AD 6 Occipital Ctx	27.2
Control (Path) 3 Hippo	4.3	Control 1 Occipital Ctx	2.4
AD 1 Temporal Ctx	7.7	Control 2 Occipital Ctx	30.1
AD 2 Temporal Ctx	17.4	Control 3 Occipital Ctx	8.0
AD 3 Temporal Ctx	5.7	Control 4 Occipital Ctx	4.8
AD 4 Temporal Ctx	10.6	Control (Path) 1 Occipital Ctx	51.1
AD 5 Inf Temporal Ctx	67.8	Control (Path) 2 Occipital Ctx	4.8
AD 5 Sup Temporal Ctx	33.9	Control (Path) 3 Occipital	0.6

		Ctx	
AD 6 Inf Temporal Ctx	23.7	Control (Path) 4 Occipital Ctx	10.7
AD 6 Sup Temporal Ctx	17.2	Control 1 Parietal Ctx	3.2
Control 1 Temporal Ctx	3.9	Control 2 Parietal Ctx	9.7
Control 2 Temporal Ctx	23.8	Control 3 Parietal Ctx	6.9
Control 3 Temporal Ctx	4.2	Control (Path) 1 Parietal Ctx	38.4
Control 4 Temporal Ctx	4.4	Control (Path) 2 Parietal Ctx	11.0
Control (Path) 1 Temporal Ctx	37.4	Control (Path) 3 Parietal Ctx	2.6
Control (Path) 2 Temporal Ctx	9.3	Control (Path) 4 Parietal Ctx	30.1

Table AYC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3259, Run 214694855	Tissue Name	Rel. Exp.(%) Ag3259, Run 214694855
Adipose	4.2	Renal ca. TK-10	30.1
Melanoma* Hs688(A).T	6.8	Bladder	10.8
Melanoma* Hs688(B).T	5.1	Gastric ca. (liver met.) NCI-N87	100.0
Melanoma* M14	31.9	Gastric ca. KATO III	25.5
Melanoma* LOXIMV1	21.6	Colon ca. SW-948	2.2
Melanoma* SK-MEL-5	17.3	Colon ca. SW480	52.5
Squamous cell carcinoma SCC-4	14.9	Colon ca. * (SW480 met) SW620	42.9
Testis Pool	8.0	Colon ca. HT29	24.0
Prostate ca. * (bone met) PC-3	14.3	Colon ca. HCT-116	15.4
Prostate Pool	4.2	Colon ca. CaCo-2	88.9
Placenta	6.9	Colon cancer tissue	23.3
Uterus Pool	1.2	Colon ca. SW1116	3.0
Ovarian ca. OVCAR-3	9.7	Colon ca. Colo-205	8.0
Ovarian ca. SK-OV-3	6.1	Colon ca. SW-48	3.7
Ovarian ca. OVCAR-4	6.4	Colon Pool	6.4
Ovarian ca. OVCAR-5	62.4	Small Intestine Pool	4.5
Ovarian ca. IGROV-1	15.8	Stomach Pool	3.7
Ovarian ca. OVCAR-8	4.4	Bone Marrow Pool	2.6
Ovary	6.2	Fetal Heart	12.2
Breast ca. MCF-7	94.6	Heart Pool	1.0
Breast ca. MDA-MB-231	32.5	Lymph Node Pool	5.8
Breast ca. BT 549	63.7	Fetal Skeletal Muscle	4.2
Breast ca. T47D	34.4	Skeletal Muscle Pool	5.1
Breast ca. MDA-N	17.4	Spleen Pool	9.7
Breast Pool	8.5	Thymus Pool	14.4
Trachea	10.3	CNS cancer (glio/astro) U87-MG	42.9
Lung	2.0	CNS cancer (glio/astro) U-118-MG	17.3
Fetal Lung	21.2	CNS cancer (neuro;met) SK-N-AS	26.8
Lung ca. NCI-N417	5.4	CNS cancer (astro) SF-539	14.9
Lung ca. LX-1	48.3	CNS cancer (astro) SNB-75	22.1
Lung ca. NCI-H146	9.1	CNS cancer (glio) SNB-19	3.7
Lung ca. SHP-77	17.3	CNS cancer (glio) SF-295	24.5

Lung ca. A549	13.3	Brain (Amygdala) Pool	6.6
Lung ca. NCI-H526	4.4	Brain (cerebellum)	14.0
Lung ca. NCI-H23	39.0	Brain (fetal)	24.5
Lung ca. NCI-H460	7.6	Brain (Hippocampus) Pool	8.1
Lung ca. HOP-62	9.9	Cerebral Cortex Pool	11.9
Lung ca. NCI-H522	16.2	Brain (Substantia nigra) Pool	7.4
Liver	0.9	Brain (Thalamus) Pool	6.3
Fetal Liver	5.0	Brain (whole)	8.2
Liver ca. HepG2	33.0	Spinal Cord Pool	5.8
Kidney Pool	3.5	Adrenal Gland	24.8
Fetal Kidney	15.2	Pituitary gland Pool	5.3
Renal ca. 786-0	20.2	Salivary Gland	4.4
Renal ca. A498	17.2	Thyroid (female)	2.1
Renal ca. ACHN	17.3	Pancreatic ca. CAPAN2	18.6
Renal ca. UO-31	46.3	Pancreas Pool	10.4

Table AYD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3259, Run 164537290	Tissue Name	Rel. Exp.(%) Ag3259, Run 164537290
Secondary Th1 act	22.5	HUVEC IL-1beta	13.5
Secondary Th2 act	20.6	HUVEC IFN gamma	50.0
Secondary Tr1 act	23.3	HUVEC TNF alpha + IFN gamma	21.6
Secondary Th1 rest	7.7	HUVEC TNF alpha + IL4	15.4
Secondary Th2 rest	9.9	HUVEC IL-11	27.0
Secondary Tr1 rest	12.8	Lung Microvascular EC none	24.5
Primary Th1 act	9.4	Lung Microvascular EC TNFalpha + IL-1beta	24.3
Primary Th2 act	9.5	Microvascular Dermal EC none	46.3
Primary Tr1 act	12.5	Microvascular Dermal EC TNFalpha + IL-1beta	22.2
Primary Th1 rest	56.3	Bronchial epithelium TNFalpha + IL1beta	27.5
Primary Th2 rest	26.1	Small airway epithelium none	9.6
Primary Tr1 rest	19.2	Small airway epithelium TNFalpha + IL-1beta	50.0
CD45RA CD4 lymphocyte act	9.9	Coronary artery SMC rest	13.0
CD45RO CD4 lymphocyte act	24.0	Coronary artery SMC TNFalpha + IL-1beta	6.6
CD8 lymphocyte act	11.9	Astrocytes rest	6.2
Secondary CD8 lymphocyte rest	13.8	Astrocytes TNFalpha + IL-1beta	5.0
Secondary CD8 lymphocyte act	10.5	KU-812 (Basophil) rest	28.7
CD4 lymphocyte none	9.1	KU-812 (Basophil) PMA/ionomycin	100.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	22.8	CCD1106 (Keratinocytes) none	24.5
LAK cells rest	1.6	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	12.9
LAK cells IL-2	21.0	Liver cirrhosis	3.4
LAK cells IL-2+IL-12	17.3	Lupus kidney	4.1
LAK cells IL-2+IFN gamma	28.5	NCI-H292 none	31.4
LAK cells IL-2+ IL-18	27.9	NCI-H292 IL-4	22.7
LAK cells PMA/ionomycin	7.1	NCI-H292 IL-9	28.5
NK Cells IL-2 rest	16.5	NCI-H292 IL-13	11.2

Two Way MLR 3 day	18.8	NCI-H292 IFN gamma	15.1
Two Way MLR 5 day	9.7	HPAEC none	24.1
Two Way MLR 7 day	9.3	HPAEC TNF alpha + IL-1 beta	17.8
PBMC rest	8.2	Lung fibroblast none	7.1
PBMC PWM	52.9	Lung fibroblast TNF alpha + IL-1 beta	10.3
PBMC PHA-L	24.8	Lung fibroblast IL-4	10.3
Ramos (B cell) none	24.1	Lung fibroblast IL-9	12.5
Ramos (B cell) ionomycin	81.8	Lung fibroblast IL-13	8.3
B lymphocytes PWM	49.0	Lung fibroblast IFN gamma	16.8
B lymphocytes CD40L and IL-4	27.0	Dermal fibroblast CCD1070 rest	22.8
EOL-1 dbcAMP	15.4	Dermal fibroblast CCD1070 TNF alpha	45.4
EOL-1 dbcAMP PMA/ionomycin	24.5	Dermal fibroblast CCD1070 IL-1 beta	12.6
Dendritic cells none	18.6	Dermal fibroblast IFN gamma	9.3
Dendritic cells LPS	10.4	Dermal fibroblast IL-4	16.6
Dendritic cells anti-CD40	14.1	IBD Colitis 2	2.6
Monocytes rest	11.0	IBD Crohn's	3.5
Monocytes LPS	7.3	Colon	13.9
Macrophages rest	19.3	Lung	11.8
Macrophages LPS	11.7	Thymus	29.1
HUVEC none	30.6	Kidney	41.8
HUVEC starved	63.7		

CNS_neurodegeneration_v1.0 Summary: [Ag3259](#) This panel confirms the expression of the CG57505-01 gene at moderate levels in the brains of an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: [Ag3259](#) Expression of the CG57505-01 gene is highest in a gastric cancer cell line (CT = 25.6). Interestingly, expression of this gene appears to be higher in cancer cell lines than in normal tissues. Specifically, CG57505-01 gene expression appears to be upregulated in colon, gastric, renal, lung and breast cancer cell lines. Therefore, therapeutic modulation of the activity of this gene or its protein product, through the use of small molecule drugs, protein therapeutics or antibodies, might be beneficial in the treatment of these cancers.

In addition, this gene is expressed at moderate levels in all regions of the central nervous system examined, including in amygdala, hippocampus, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

CNS_neurodegeneration_v1.0 Summary: Ag3251 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3251 Results from one experiment with the CG57473-01 gene are not included. The amp plot indicates that there were experimental difficulties with this run.

Panel 4D Summary: Ag3251 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV63

Expression of NOV63/CG57777-01 was assessed using the primer-probe set Ag3327, described in Table BFA. Results of the RTQ-PCR runs are shown in Tables BFB, BFC and BFD.

Table BFA. Probe Name Ag3327

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ttctgtgaaccaatgagaaca-3'	22	424	440
Probe	TET-5'-cacaacgtaccagaatttctgggaca-3'-TAMRA	26	450	441
Reverse	5'-ccctctaaccactgcttagct-3'	22	477	442

Table BFB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3327, Run 210138310	Rel. Exp.(%) Ag3327, Run 224063127	Tissue Name	Rel. Exp.(%) Ag3327, Run 210138310	Rel. Exp.(%) Ag3327, Run 224063127
AD 1 Hippo	6.1	6.0	Control (Path) 3 Temporal Ctx	14.0	12.3
AD 2 Hippo	28.1	29.3	Control (Path) 4 Temporal Ctx	69.7	63.7
AD 3 Hippo	14.9	13.5	AD 1 Occipital Ctx	18.8	31.4
AD 4 Hippo	24.7	15.9	AD 2 Occipital Ctx (Missing)	0.0	0.0
AD 5 Hippo	59.0	65.1	AD 3 Occipital Ctx	17.1	9.1
AD 6 Hippo	45.7	52.5	AD 4 Occipital Ctx	48.0	35.8
Control 2 Hippo	38.2	28.7	AD 5 Occipital Ctx	52.9	0.0
Control 4 Hippo	15.5	16.4	AD 6 Occipital Ctx	23.0	40.1
Control (Path) 3 Hippo	11.7	2.5	Control 1 Occipital Ctx	1.2	2.1
AD 1 Temporal Ctx	16.3	14.2	Control 2 Occipital Ctx	31.6	59.0
AD 2 Temporal Ctx	21.9	29.5	Control 3 Occipital Ctx	62.9	60.3
AD 3 Temporal Ctx	15.1	12.2	Control 4 Occipital Ctx	10.2	6.9
AD 4 Temporal	24.7	16.0	Control (Path) 1	100.0	96.6

Ctx			Occipital Ctx		
AD 5 Inf Temporal Ctx	85.9	41.8	Control (Path) 2 Occipital Ctx	44.1	10.0
AD 5 Sup Temporal Ctx	47.3	59.9	Control (Path) 3 Occipital Ctx	1.7	2.0
AD 6 Inf Temporal Ctx	57.4	61.6	Control (Path) 4 Occipital Ctx	55.5	41.2
AD 6 Sup Temporal Ctx	77.9	70.7	Control 1 Parietal Ctx	9.0	7.1
Control 1 Temporal Ctx	14.3	13.6	Control 2 Parietal Ctx	52.9	67.8
Control 2 Temporal Ctx	34.9	18.8	Control 3 Parietal Ctx	15.4	10.9
Control 3 Temporal Ctx	42.6	28.1	Control (Path) 1 Parietal Ctx	84.1	77.4
Control 3 Temporal Ctx	19.6	13.1	Control (Path) 2 Parietal Ctx	43.8	58.6
Control (Path) 1 Temporal Ctx	75.8	100.0	Control (Path) 3 Parietal Ctx	9.2	9.0
Control (Path) 2 Temporal Ctx	98.6	72.7	Control (Path) 4 Parietal Ctx	89.5	75.8

Table BFC. General screening panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3327, Run 215678614	Tissue Name	Rel. Exp.(%) Ag3327, Run 215678614
Adipose	2.3	Renal ca. TK-10	13.3
Melanoma* Hs688(A).T	2.8	Bladder	17.1
Melanoma* Hs688(B).T	1.1	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	0.0	Gastric ca. KATO III	1.2
Melanoma* LOXIMVI	0.7	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.6	Colon ca. SW480	8.1
Squamous cell carcinoma SCC-4	2.0	Colon ca.* (SW480 met) SW620	0.0
Testis Pool	15.1	Colon ca. HT29	1.5
Prostate ca.* (bone met) PC-3	0.6	Colon ca. HCT-116	8.2
Prostate Pool	1.6	Colon ca. CaCo-2	6.1
Placenta	0.0	Colon cancer tissue	0.0
Uterus Pool	0.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	1.6	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	1.3	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	1.5	Colon Pool	0.0
Ovarian ca. OVCAR-5	7.8	Small Intestine Pool	0.7
Ovarian ca. IGROV-1	0.0	Stomach Pool	4.1
Ovarian ca. OVCAR-8	1.1	Bone Marrow Pool	1.0
Ovary	4.6	Fetal Heart	0.0
Breast ca. MCF-7	0.0	Heart Pool	0.0
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	0.6
Breast ca. BT 549	9.2	Fetal Skeletal Muscle	0.0
Breast ca. T47D	1.5	Skeletal Muscle Pool	3.5
Breast ca. MDA-N	0.0	Spleen Pool	1.4
Breast Pool	14.4	Thymus Pool	2.2
Trachea	0.0	CNS cancer (glio/astro) U87-MG	13.2
Lung	16.7	CNS cancer (glio/astro) U-118-MG	0.0

Fetal Lung	15.6	CNS cancer (neuro;met) SK-N-AS	1.3
Lung ca. NCI-N417	1.8	CNS cancer (astro) SF-539	1.3
Lung ca. LX-1	2.0	CNS cancer (astro) SNB-75	100.0
Lung ca. NCI-H146	1.6	CNS cancer (glio) SNB-19	2.7
Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	39.8
Lung ca. A549	12.7	Brain (Amygdala) Pool	4.3
Lung ca. NCI-H526	1.4	Brain (cerebellum)	8.7
Lung ca. NCI-H23	3.1	Brain (fetal)	0.6
Lung ca. NCI-H460	8.4	Brain (Hippocampus) Pool	3.0
Lung ca. HOP-62	0.9	Cerebral Cortex Pool	12.0
Lung ca. NCI-H522	1.2	Brain (Substantia nigra) Pool	3.9
Liver	0.0	Brain (Thalamus) Pool	25.9
Fetal Liver	0.0	Brain (whole)	8.8
Liver ca. HepG2	0.8	Spinal Cord Pool	0.8
Kidney Pool	0.0	Adrenal Gland	0.0
Fetal Kidney	0.7	Pituitary gland Pool	1.3
Renal ca. 786-0	21.5	Salivary Gland	0.0
Renal ca. A498	11.8	Thyroid (female)	3.1
Renal ca. ACHN	1.1	Pancreatic ca. CAPAN2	1.2
Renal ca. UO-31	2.7	Pancreas Pool	6.3

Table BFD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3327, Run 165021004	Tissue Name	Rel. Exp.(%) Ag3327, Run 165021004
Secondary Th1 act	11.3	HUVEC IL-1beta	4.0
Secondary Th2 act	12.5	HUVEC IFN gamma	12.3
Secondary Tr1 act	17.9	HUVEC TNF alpha + IFN gamma	2.3
Secondary Th1 rest	4.4	HUVEC TNF alpha + IL4	1.8
Secondary Th2 rest	6.0	HUVEC IL-11	6.5
Secondary Tr1 rest	6.4	Lung Microvascular EC none	8.5
Primary Th1 act	20.6	Lung Microvascular EC TNFalpha + IL-1beta	31.6
Primary Th2 act	13.8	Microvascular Dermal EC none	17.9
Primary Tr1 act	17.1	Microvascular Dermal EC TNFalpha + IL-1beta	29.7
Primary Th1 rest	25.5	Bronchial epithelium TNFalpha + IL1beta	4.2
Primary Th2 rest	11.7	Small airway epithelium none	2.0
Primary Tr1 rest	4.6	Small airway epithelium TNFalpha + IL-1beta	13.2
CD45RA CD4 lymphocyte act	9.3	Coronary artery SMC rest	9.2
CD45RO CD4 lymphocyte act	12.9	Coronary artery SMC TNFalpha + IL-1beta	2.4
CD8 lymphocyte act	14.9	Astrocytes rest	12.5
Secondary CD8 lymphocyte rest	11.1	Astrocytes TNFalpha + IL-1beta	9.9
Secondary CD8 lymphocyte act	13.2	KU-812 (Basophil) rest	7.1
CD4 lymphocyte none	5.8	KU-812 (Basophil) PMA/ionomycin	21.5
2ry Th1/Th2/Tr1_anti-CD95 CH11	6.3	CCD1106 (Keratinocytes) none	7.1
LAK cells rest	12.8	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	2.2

LAK cells IL-2	0.0	Liver cirrhosis	17.7
LAK cells IL-2+IL-12	11.1	Lupus kidney	19.3
LAK cells IL-2+IFN gamma	12.2	NCI-H292 none	27.7
LAK cells IL-2+ IL-18	6.3	NCI-H292 IL-4	14.9
LAK cells PMA/ionomycin	8.2	NCI-H292 IL-9	14.8
NK Cells IL-2 rest	9.4	NCI-H292 IL-13	2.7
Two Way MLR 3 day	8.3	NCI-H292 IFN gamma	3.0
Two Way MLR 5 day	4.0	HPAEC none	1.4
Two Way MLR 7 day	11.6	HPAEC TNF alpha + IL-1 beta	1.2
PBMC rest	5.0	Lung fibroblast none	7.6
PBMC PWM	73.2	Lung fibroblast TNF alpha + IL-1 beta	9.0
PBMC PHA-L	16.2	Lung fibroblast IL-4	9.5
Ramos (B cell) none	22.5	Lung fibroblast IL-9	10.7
Ramos (B cell) ionomycin	100.0	Lung fibroblast IL-13	8.4
B lymphocytes PWM	23.8	Lung fibroblast IFN gamma	9.5
B lymphocytes CD40L and IL-4	11.0	Dermal fibroblast CCD1070 rest	17.3
EOL-1 dbcAMP	2.1	Dermal fibroblast CCD1070 TNF alpha	35.8
EOL-1 dbcAMP PMA/ionomycin	2.1	Dermal fibroblast CCD1070 IL-1 beta	14.0
Dendritic cells none	2.9	Dermal fibroblast IFN gamma	5.1
Dendritic cells LPS	6.3	Dermal fibroblast IL-4	8.1
Dendritic cells anti-CD40	3.7	IBD Colitis 2	5.3
Monocytes rest	12.6	IBD Crohn's	4.5
Monocytes LPS	13.5	Colon	9.3
Macrophages rest	5.1	Lung	7.7
Macrophages LPS	9.2	Thymus	62.4
HUVEC none	3.8	Kidney	7.4
HUVEC starved	4.9		

CNS_neurodegeneration_v1.0 Summary: [Ag3327](#) This panel confirms the expression of the CG57777-01 gene at low levels in the brain in an independent group of individuals. This gene is found to be down-regulated in the temporal cortex of Alzheimer's disease patients. Therefore, up-regulation of this gene or its protein product, or treatment with specific agonists for this receptor may be of use in reversing the dementia/memory loss associated with this disease and neuronal death.

General_screening_panel_v1.4 Summary: [Ag3327](#) The CG57777-01 codes for a homologue of LINE-1 reverse transcriptase. This gene is moderately expressed in samples derived from two of the CNS cancer cell line. Thus, the expression of this gene could be used to distinguish these samples from the other samples in the panel.

Panel 4D Summary: [Ag3327](#) The CG57777-01 gene is expressed at low to moderate levels in a wide range of cell types of significance in the immune response in health and disease. These cells include members of the T-cell, B-cell, endothelial cell, macrophage/monocyte, and peripheral blood mononuclear cell family, as well as epithelial and

fibroblast cell types from lung and skin, and normal tissues represented by colon, lung, thymus and kidney. This ubiquitous pattern of expression suggests that this gene product may be involved in homeostatic processes for these and other cell types and tissues.

This pattern is in agreement with the expression profile in

5 General_screening_panel_v1.5 and also suggests a role for the gene product in cell survival and proliferation.

Therefore, modulation of the gene product with a functional therapeutic may lead to the alteration of functions associated with these cell types and lead to improvement of the symptoms of patients suffering from autoimmune and inflammatory diseases such as asthma,
10 allergies, inflammatory bowel disease, lupus erythematosus, psoriasis, rheumatoid arthritis, and osteoarthritis.

NOV64

Expression of NOV64/CG57779-01 was assessed using the primer-probe set Ag3328, described in Table BGA. Results of the RTQ-PCR runs are shown in Tables BGB, BGC and
15 BGD.

Table BGA. Probe Name Ag3328

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gatgaagctggaaccatcat-3'	21	2994	443
Probe	TET-5'-tcacaaggacagaaaccaaacactg-3'-TAMRA	26	3028	444
Reverse	5'-cccacctatgagtgaacatg-3'	22	3054	445

Table BGB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3328, Run 210138311	Tissue Name	Rel. Exp.(%) Ag3328, Run 210138311
AD 1 Hippo	9.4	Control (Path) 3 Temporal Ctx	5.8
AD 2 Hippo	22.7	Control (Path) 4 Temporal Ctx	30.8
AD 3 Hippo	6.6	AD 1 Occipital Ctx	19.1
AD 4 Hippo	7.8	AD 2 Occipital Ctx (Missing)	0.5
AD 5 hippo	91.4	AD 3 Occipital Ctx	6.1
AD 6 Hippo	50.3	AD 4 Occipital Ctx	14.4
Control 2 Hippo	17.7	AD 5 Occipital Ctx	3.6
Control 4 Hippo	9.7	AD 6 Occipital Ctx	22.5
Control (Path) 3 Hippo	5.5	Control 1 Occipital Ctx	3.6
AD 1 Temporal Ctx	15.4	Control 2 Occipital Ctx	27.2
AD 2 Temporal Ctx	22.8	Control 3 Occipital Ctx	21.2
AD 3 Temporal Ctx	5.6	Control 4 Occipital Ctx	6.9
AD 4 Temporal Ctx	14.7	Control (Path) 1 Occipital Ctx	76.8
AD 5 Inf Temporal Ctx	100.0	Control (Path) 2 Occipital	9.5

		Ctx	
AD 5 SupTemporal Ctx	68.8	Control (Path) 3 Occipital Ctx	2.6
AD 6 Inf Temporal Ctx	47.6	Control (Path) 4 Occipital Ctx	22.2
AD 6 Sup Temporal Ctx	55.9	Control 1 Parietal Ctx	5.0
Control 1 Temporal Ctx	5.4	Control 2 Parietal Ctx	53.2
Control 2 Temporal Ctx	11.7	Control 3 Parietal Ctx	12.9
Control 3 Temporal Ctx	10.1	Control (Path) 1 Parietal Ctx	49.7
Control 4 Temporal Ctx	7.3	Control (Path) 2 Parietal Ctx	22.5
Control (Path) 1 Temporal Ctx	42.9	Control (Path) 3 Parietal Ctx	7.4
Control (Path) 2 Temporal Ctx	34.6	Control (Path) 4 Parietal Ctx	46.3

Table BGC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3328, Run 215678615	Tissue Name	Rel. Exp.(%) Ag3328, Run 215678615
Adipose	20.0	Renal ca. TK-10	27.2
Melanoma* Hs688(A).T	18.9	Bladder	39.8
Melanoma* Hs688(B).T	14.0	Gastric ca. (liver met.) NCI-N87	48.0
Melanoma* M14	11.6	Gastric ca. KATO III	25.5
Melanoma* LOXIMVI	13.3	Colon ca. SW-948	3.6
Melanoma* SK-MEL-5	28.1	Colon ca. SW480	33.9
Squamous cell carcinoma SCC-4	11.0	Colon ca.* (SW480 met) SW620	24.1
Testis Pool	15.7	Colon ca. HT29	12.7
Prostate ca.* (bone met) PC-3	24.1	Colon ca. HCT-116	24.5
Prostate Pool	12.3	Colon ca. CaCo-2	28.7
Placenta	6.1	Colon cancer tissue	20.7
Uterus Pool	7.3	Colon ca. SW1116	6.7
Ovarian ca. OVCAR-3	33.7	Colon ca. Colo-205	3.7
Ovarian ca. SK-OV-3	69.3	Colon ca. SW-48	3.5
Ovarian ca. OVCAR-4	10.4	Colon Pool	41.2
Ovarian ca. OVCAR-5	54.0	Small Intestine Pool	51.4
Ovarian ca. IGROV-1	16.4	Stomach Pool	5.2
Ovarian ca. OVCAR-8	11.3	Bone Marrow Pool	22.7
Ovary	15.1	Fetal Heart	34.2
Breast ca. MCF-7	25.3	Heart Pool	16.2
Breast ca. MDA-MB-231	29.1	Lymph Node Pool	44.1
Breast ca. BT 549	33.0	Fetal Skeletal Muscle	26.1
Breast ca. T47D	44.4	Skeletal Muscle Pool	7.7
Breast ca. MDA-N	17.7	Spleen Pool	21.5
Breast Pool	2.4	Thymus Pool	33.2
Trachea	26.1	CNS cancer (glio/astro) U87-MG	23.5
Lung	27.0	CNS cancer (glio/astro) U-118-MG	38.4
Fetal Lung	100.0	CNS cancer (neuro;met) SK-N-AS	27.7
Lung ca. NCI-N417	1.4	CNS cancer (astro) SF-539	12.5
Lung ca. LX-1	35.4	CNS cancer (astro) SNB-75	59.9

LAK cells PMA/ionomycin	11.0	NCI-H292 IL-9	22.1
NK Cells IL-2 rest	18.4	NCI-H292 IL-13	13.1
Two Way MLR 3 day	23.2	NCI-H292 IFN gamma	18.7
Two Way MLR 5 day	8.8	HPAEC none	8.7
Two Way MLR 7 day	10.8	HPAEC TNF alpha + IL-1 beta	18.7
PBMC rest	9.9	Lung fibroblast none	9.6
PBMC PWM	48.3	Lung fibroblast TNF alpha + IL-1 beta	6.3
PBMC PHA-L	16.7	Lung fibroblast IL-4	20.3
Ramos (B cell) none	19.3	Lung fibroblast IL-9	13.8
Ramos (B cell) ionomycin	43.8	Lung fibroblast IL-13	14.9
B lymphocytes PWM	19.3	Lung fibroblast IFN gamma	15.7
B lymphocytes CD40L and IL-4	22.7	Dermal fibroblast CCD1070 rest	24.0
EOL-1 dbcAMP	12.2	Dermal fibroblast CCD1070 TNF alpha	50.7
EOL-1 dbcAMP PMA/ionomycin	15.2	Dermal fibroblast CCD1070 IL-1 beta	11.4
Dendritic cells none	10.5	Dermal fibroblast IFN gamma	12.5
Dendritic cells LPS	12.5	Dermal fibroblast IL-4	21.8
Dendritic cells anti-CD40	10.8	IBD Colitis 2	8.3
Monocytes rest	19.9	IBD Crohn's	7.2
Monocytes LPS	13.9	Colon	30.4
Macrophages rest	20.4	Lung	17.0
Macrophages LPS	7.9	Thymus	84.7
HUVEC none	8.2	Kidney	100.0
HUVEC starved	10.0		

CNS_neurodegeneration_v1.0 Summary: Ag3328 This panel confirms the expression of CG57779-01 gene at low levels in the brains of an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment.

General_screening_panel_v1.4 Summary: Ag3328 The CG57779-01 gene encodes a homolog of LINE-1 reverse transcriptase. Its expression is moderate to high across all of the samples on this panel. Therefore, this gene may be playing an important role in cellular function

Panel 4D Summary: Ag3328 The CG57779-01 gene is expressed at high to moderate levels in a wide range of cell types of significance in the immune response in health and disease. These cells include members of the T-cell, B-cell, endothelial cell, macrophage/monocyte, and peripheral blood mononuclear cell family, as well as epithelial and fibroblast cell types from lung and skin, and normal tissues represented by colon, lung, thymus and kidney. This ubiquitous pattern of expression suggests that this gene product may be involved in homeostatic processes for these and other cell types and tissues.

This pattern is in agreement with the expression profile in General_screening_panel_v1.4 and also suggests a role for the gene product in cell survival and proliferation.

Therefore, modulation of the gene product with a functional therapeutic may lead to the alteration of functions associated with these cell types and lead to improvement of the symptoms of patients suffering from autoimmune and inflammatory diseases such as asthma, allergies, inflammatory bowel disease, lupus erythematosus, psoriasis, rheumatoid arthritis, and osteoarthritis.

NOV65

Expression of NOV65/CG57781-01 was assessed using the primer-probe set Ag3329, described in Table BHA. Results of the RTQ-PCR runs are shown in Tables BHB, BHC and BHD.

Table BHA. Probe Name Ag3329

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-tcacaaggacagaaaaccaac-3'	22	2944	446
Probe	TET-5'-ccacatgttctcactcataggtggga-3'-TAMRA	26	2967	447
Reverse	5'-gtgtccatgtgttctcgttgtt-3'	22	2997	448

Table BHB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3329, Run 210146230	Tissue Name	Rel. Exp.(%) Ag3329, Run 210146230
AD 1 Hippo	9.2	Control (Path) 3 Temporal Ctx	6.4
AD 2 Hippo	19.9	Control (Path) 4 Temporal Ctx	35.4
AD 3 Hippo	10.0	AD 1 Occipital Ctx	20.3
AD 4 Hippo	10.0	AD 2 Occipital Ctx (Missing)	0.1
AD 5 Hippo	64.6	AD 3 Occipital Ctx	6.4
AD 6 Hippo	42.9	AD 4 Occipital Ctx	18.6
Control 2 Hippo	20.4	AD 5 Occipital Ctx	16.0
Control 4 Hippo	10.7	AD 6 Occipital Ctx	18.0
Control (Path) 3 Hippo	5.5	Control 1 Occipital Ctx	3.1
AD 1 Temporal Ctx	20.4	Control 2 Occipital Ctx	28.7
AD 2 Temporal Ctx	23.7	Control 3 Occipital Ctx	24.1
AD 3 Temporal Ctx	8.7	Control 4 Occipital Ctx	6.0
AD 4 Temporal Ctx	19.9	Control (Path) 1 Occipital Ctx	75.3
AD 5 Inf Temporal Ctx	100.0	Control (Path) 2 Occipital Ctx	13.2
AD 5 Sup Temporal Ctx	65.5	Control (Path) 3 Occipital Ctx	3.0
AD 6 Inf Temporal Ctx	46.3	Control (Path) 4 Occipital Ctx	0.0
AD 6 Sup Temporal Ctx	62.0	Control 1 Parietal Ctx	5.4

Control 1 Temporal Ctx	5.7	Control 2 Parietal Ctx	43.8
Control 2 Temporal Ctx	15.7	Control 3 Parietal Ctx	11.8
Control 3 Temporal Ctx	16.6	Control (Path) 1 Parietal Ctx	47.0
Control 3 Temporal Ctx	10.3	Control (Path) 2 Parietal Ctx	23.0
Control (Path) 1 Temporal Ctx	50.0	Control (Path) 3 Parietal Ctx	5.9
Control (Path) 2 Temporal Ctx	44.1	Control (Path) 4 Parietal Ctx	39.5

Table BHC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3329, Run 215678554	Tissue Name	Rel. Exp.(%) Ag3329, Run 215678554
Adipose	18.4	Renal ca. TK-10	31.0
Melanoma* Hs688(A).T	15.3	Bladder	48.0
Melanoma* Hs688(B).T	13.7	Gastric ca. (liver met.) NCI-N87	38.4
Melanoma* M14	21.3	Gastric ca. KATO III	22.2
Melanoma* LOXIMVI	15.8	Colon ca. SW-948	4.3
Melanoma* SK-MEL-5	39.0	Colon ca. SW480	38.4
Squamous cell carcinoma SCC-4	17.9	Colon ca.* (SW480 met) SW620	21.9
Testis Pool	10.4	Colon ca. HT29	15.7
Prostate ca.* (bone met) PC-3	31.0	Colon ca. HCT-116	21.3
Prostate Pool	18.8	Colon ca. CaCo-2	27.5
Placenta	4.4	Colon cancer tissue	17.1
Uterus Pool	12.6	Colon ca. SW1116	5.2
Ovarian ca. OVCAR-3	22.7	Colon ca. Colo-205	3.8
Ovarian ca. SK-OV-3	34.9	Colon ca. SW-48	3.3
Ovarian ca. OVCAR-4	5.6	Colon Pool	79.0
Ovarian ca. OVCAR-5	44.8	Small Intestine Pool	59.9
Ovarian ca. IGROV-1	15.8	Stomach Pool	48.3
Ovarian ca. OVCAR-8	11.7	Bone Marrow Pool	39.8
Ovary	19.2	Fetal Heart	67.8
Breast ca. MCF-7	26.4	Heart Pool	22.8
Breast ca. MDA-MB-231	25.0	Lymph Node Pool	91.4
Breast ca. BT 549	48.3	Fetal Skeletal Muscle	30.1
Breast ca. T47D	49.3	Skeletal Muscle Pool	29.7
Breast ca. MDA-N	16.3	Spleen Pool	28.7
Breast Pool	76.3	Thymus Pool	59.9
Trachea	32.5	CNS cancer (glio/astro) U87-MG	32.5
Lung	26.2	CNS cancer (glio/astro) U-118-MG	40.3
Fetal Lung	89.5	CNS cancer (neuro;met) SK-N-AS	35.4
Lung ca. NCI-N417	22.7	CNS cancer (astro) SF-539	11.0
Lung ca. LX-1	28.3	CNS cancer (astro) SNB-75	54.3
Lung ca. NCI-H146	10.6	CNS cancer (glio) SNB-19	9.9
Lung ca. SHP-77	26.8	CNS cancer (glio) SF-295	81.2
Lung ca. A549	23.2	Brain (Amygdala) Pool	19.3
Lung ca. NCI-H526	4.7	Brain (cerebellum)	21.0
Lung ca. NCI-H23	54.3	Brain (fetal)	47.0
Lung ca. NCI-H460	46.0	Brain (Hippocampus) Pool	20.0

Lung ca. HOP-62	18.2	Cerebral Cortex Pool	21.6
Lung ca. NCI-H522	35.4	Brain (Substantia nigra) Pool	14.5
Liver	0.5	Brain (Thalamus) Pool	35.6
Fetal Liver	17.1	Brain (whole)	18.4
Liver ca. HepG2	19.6	Spinal Cord Pool	20.6
Kidney Pool	100.0	Adrenal Gland	21.0
Fetal Kidney	98.6	Pituitary gland Pool	11.1
Renal ca. 786-0	27.5	Salivary Gland	5.4
Renal ca. A498	9.9	Thyroid (female)	4.4
Renal ca. ACHN	23.3	Pancreatic ca. CAPAN2	39.5
Renal ca. UO-31	31.9	Pancreas Pool	56.6

Table BHD. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3329, Run 165021015	Tissue Name	Rel. Exp.(%) Ag3329, Run 165021015
Secondary Th1 act	27.4	HUVEC IL-1beta	10.4
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	25.0	HUVEC TNF alpha + IFN gamma	6.6
Secondary Th1 rest	7.5	HUVEC TNF alpha + IL4	5.8
Secondary Th2 rest	10.2	HUVEC IL-11	5.4
Secondary Tr1 rest	12.7	Lung Microvascular EC none	7.9
Primary Th1 act	24.0	Lung Microvascular EC TNFalpha + IL-1beta	9.9
Primary Th2 act	21.6	Microvascular Dermal EC none	9.5
Primary Tr1 act	27.9	Microvascular Dermal EC TNFalpha + IL-1beta	8.5
Primary Th1 rest	39.0	Bronchial epithelium TNFalpha + IL1beta	8.1
Primary Th2 rest	17.8	Small airway epithelium none	2.1
Primary Tr1 rest	20.7	Small airway epithelium TNFalpha + IL-1beta	16.5
CD45RA CD4 lymphocyte act	10.7	Coronary artery SMC rest	5.4
CD45RO CD4 lymphocyte act	21.0	Coronary artery SMC TNFalpha + IL-1beta	2.7
CD8 lymphocyte act	11.3	Astrocytes rest	7.4
Secondary CD8 lymphocyte rest	11.8	Astrocytes TNFalpha + IL-1beta	6.7
Secondary CD8 lymphocyte act	9.9	KU-812 (Basophil) rest	9.4
CD4 lymphocyte none	11.5	KU-812 (Basophil) PMA/ionomycin	49.7
2ry Th1/Th2/Tr1_anti-CD95 CH11	26.4	CCD1106 (Keratinocytes) none	6.7
LAK cells rest	24.5	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	4.0
LAK cells IL-2	22.4	Liver cirrhosis	36.6
LAK cells IL-2+IL-12	10.5	Lupus kidney	11.3
LAK cells IL-2+IFN gamma	14.1	NCI-H292 none	27.9
LAK cells IL-2+ IL-18	15.3	NCI-H292 IL-4	20.2
LAK cells PMA/ionomycin	15.4	NCI-H292 IL-9	26.2
NK Cells IL-2 rest	17.7	NCI-H292 IL-13	17.8
Two Way MLR 3 day	15.6	NCI-H292 IFN gamma	13.3
Two Way MLR 5 day	7.8	HPAEC none	6.5
Two Way MLR 7 day	7.5	HPAEC TNF alpha + IL-1 beta	12.6
PBMC rest	3.9	Lung fibroblast none	6.3

PBMC PWM	57.8	Lung fibroblast TNF alpha + IL-1 beta	3.8
PBMC PHA-L	19.3	Lung fibroblast IL-4	11.2
Ramos (B cell) none	20.3	Lung fibroblast IL-9	9.4
Ramos (B cell) ionomycin	42.9	Lung fibroblast IL-13	15.9
B lymphocytes PWM	19.6	Lung fibroblast IFN gamma	12.9
B lymphocytes CD40L and IL-4	27.5	Dermal fibroblast CCD1070 rest	20.3
EOL-1 dbcAMP	3.7	Dermal fibroblast CCD1070 TNF alpha	73.7
EOL-1 dbcAMP PMA/ionomycin	15.0	Dermal fibroblast CCD1070 IL-1 beta	11.6
Dendritic cells none	10.4	Dermal fibroblast IFN gamma	11.2
Dendritic cells LPS	10.1	Dermal fibroblast IL-4	20.3
Dendritic cells anti-CD40	10.4	IBD Colitis 2	8.6
Monocytes rest	15.2	IBD Crohn's	5.5
Monocytes LPS	20.9	Colon	33.4
Macrophages rest	25.2	Lung	18.3
Macrophages LPS	7.1	Thymus	87.7
HUVEC none	5.4	Kidney	100.0
HUVEC starved	11.7		

CNS_neurodegeneration_v1.0 Summary: [Ag3329](#) The CG57781-01 encodes a gene that is homologous to LINE-1 reverse transcriptase. This panel confirms the expression of this gene at low levels in the brains of an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment.

General_screening_panel_v1.4 Summary: [Ag3329](#) The CG57781-01 encodes a gene that is homologous to LINE-1 reverse transcriptase. Its expression is moderate to high across all of the samples on this panel. Interestingly, this gene is expressed at much higher levels in fetal (CT = 25.44) when compared to adult liver(CT = 30.53). This observation suggests that expression of this gene can be used to distinguish fetal from adult liver.

Panel 4D Summary: [Ag3329](#) This gene is expressed at high to moderate levels in a wide range of cell types of significance in the immune response in health and disease. These cells include members of the T-cell, B-cell, endothelial cell, macrophage/monocyte, and peripheral blood mononuclear cell family, as well as epithelial and fibroblast cell types from lung and skin, and normal tissues represented by colon, lung, thymus and kidney. This ubiquitous pattern of expression suggests that this gene product may be involved in homeostatic processes for these and other cell types and tissues.

This pattern is in agreement with the expression profile in [General_screening_panel_v1.4](#) and also suggests a role for the gene product in cell survival and proliferation.

Therefore, modulation of the gene product with a functional therapeutic may lead to the alteration of functions associated with these cell types and lead to improvement of the symptoms of patients suffering from autoimmune and inflammatory diseases such as asthma, allergies, inflammatory bowel disease, lupus erythematosus, psoriasis, rheumatoid arthritis, and osteoarthritis.

NOV66

Expression of NOV66/CG57783-01 was assessed using the primer-probe set Ag3330, described in Table BIA. Results of the RTQ-PCR runs are shown in Tables BIB, BIC, and BID.

Table BIA. Probe Name Ag3330

Primers	Sequences	Length	Start Position	Seq id no:
Forward	5'-gccatcccattactgggtatat-3'	22	2773	449
Probe	TET-5'-tcatgctgtataaagacacatgcag-3'-TAMRA	26	2812	450
Reverse	5'-tagtgccgcaataaacatacgt-3'	22	2838	451

Table BIB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3330, Run 210146231	Tissue Name	Rel. Exp.(%) Ag3330, Run 210146231
AD 1 Hippo	6.8	Control (Path) 3 Temporal Ctx	4.5
AD 2 Hippo	18.3	Control (Path) 4 Temporal Ctx	26.1
AD 3 Hippo	5.6	AD 1 Occipital Ctx	13.2
AD 4 Hippo	5.2	AD 2 Occipital Ctx (Missing)	0.2
AD 5 hippo	66.4	AD 3 Occipital Ctx	4.2
AD 6 Hippo	42.0	AD 4 Occipital Ctx	12.7
Control 2 Hippo	19.2	AD 5 Occipital Ctx	17.1
Control 4 Hippo	7.2	AD 6 Occipital Ctx	20.9
Control (Path) 3 Hippo	4.0	Control 1 Occipital Ctx	1.8
AD 1 Temporal Ctx	14.2	Control 2 Occipital Ctx	29.5
AD 2 Temporal Ctx	23.0	Control 3 Occipital Ctx	12.7
AD 3 Temporal Ctx	5.1	Control 4 Occipital Ctx	4.6
AD 4 Temporal Ctx	17.2	Control (Path) 1 Occipital Ctx	70.7
AD 5 Inf Temporal Ctx	100.0	Control (Path) 2 Occipital Ctx	11.7
AD 5 Sup Temporal Ctx	50.7	Control (Path) 3 Occipital Ctx	2.0
AD 6 Inf Temporal Ctx	51.1	Control (Path) 4 Occipital Ctx	13.1
AD 6 Sup Temporal Ctx	52.9	Control 1 Parietal Ctx	5.8
Control 1 Temporal Ctx	4.2	Control 2 Parietal Ctx	49.3
Control 2 Temporal Ctx	13.4	Control 3 Parietal Ctx	11.8
Control 3 Temporal Ctx	10.2	Control (Path) 1 Parietal Ctx	56.6
Control 4 Temporal Ctx	5.7	Control (Path) 2 Parietal	18.9

		Ctx	
Control (Path) 1 Temporal Ctx	44.1	Control (Path) 3 Parietal Ctx	3.1
Control (Path) 2 Temporal Ctx	41.2	Control (Path) 4 Parietal Ctx	34.9

Table BIC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3330, Run 215678685	Tissue Name	Rel. Exp.(%) Ag3330, Run 215678685
Adipose	27.4	Renal ca. TK-10	32.8
Melanoma* Hs688(A).T	29.1	Bladder	54.3
Melanoma* Hs688(B).T	23.7	Gastric ca. (liver met.) NCI-N87	51.1
Melanoma* M14	20.7	Gastric ca. KATO III	31.0
Melanoma* LOXIMVI	18.2	Colon ca. SW-948	5.5
Melanoma* SK-MEL-5	44.1	Colon ca. SW480	39.5
Squamous cell carcinoma SCC-4	17.2	Colon ca.* (SW480 met) SW620	29.7
Testis Pool	24.0	Colon ca. HT29	15.3
Prostate ca.* (bone met) PC-3	41.8	Colon ca. HCT-116	41.8
Prostate Pool	23.0	Colon ca. CaCo-2	44.1
Placenta	6.7	Colon cancer tissue	27.4
Uterus Pool	13.7	Colon ca. SW1116	7.6
Ovarian ca. OVCAR-3	39.0	Colon ca. Colo-205	5.3
Ovarian ca. SK-OV-3	46.3	Colon ca. SW-48	3.9
Ovarian ca. OVCAR-4	9.2	Colon Pool	68.3
Ovarian ca. OVCAR-5	63.7	Small Intestine Pool	73.7
Ovarian ca. IGROV-1	26.4	Stomach Pool	42.0
Ovarian ca. OVCAR-8	12.4	Bone Marrow Pool	34.6
Ovary	24.0	Fetal Heart	70.2
Breast ca. MCF-7	39.5	Heart Pool	33.9
Breast ca. MDA-MB-231	33.0	Lymph Node Pool	64.6
Breast ca. BT 549	49.7	Fetal Skeletal Muscle	31.6
Breast ca. T47D	58.2	Skeletal Muscle Pool	30.8
Breast ca. MDA-N	24.5	Spleen Pool	26.4
Breast Pool	56.3	Thymus Pool	44.8
Trachea	32.5	CNS cancer (glio/astro) U87-MG	44.4
Lung	43.5	CNS cancer (glio/astro) U-118-MG	58.2
Fetal Lung	100.0	CNS cancer (neuro;met) SK-N-AS	45.1
Lung ca. NCI-N417	11.8	CNS cancer (astro) SF-539	16.7
Lung ca. LX-1	42.6	CNS cancer (astro) SNB-75	59.9
Lung ca. NCI-H146	0.0	CNS cancer (glio) SNB-19	21.0
Lung ca. SHP-77	44.8	CNS cancer (glio) SF-295	71.2
Lung ca. A549	27.5	Brain (Amygdala) Pool	19.5
Lung ca. NCI-H526	7.2	Brain (cerebellum)	17.2
Lung ca. NCI-H23	57.4	Brain (fetal)	52.1
Lung ca. NCI-H460	50.3	Brain (Hippocampus) Pool	28.3
Lung ca. HOP-62	27.7	Cerebral Cortex Pool	29.5
Lung ca. NCI-H522	51.8	Brain (Substantia nigra) Pool	18.3
Liver	0.9	Brain (Thalamus) Pool	43.5
Fetal Liver	24.8	Brain (whole)	23.8

Liver ca. HepG2	17.7	Spinal Cord Pool	22.1
Kidney Pool	95.9	Adrenal Gland	23.8
Fetal Kidney	94.0	Pituitary gland Pool	11.6
Renal ca. 786-0	31.6	Salivary Gland	7.9
Renal ca. A498	15.5	Thyroid (female)	6.2
Renal ca. ACHN	28.5	Pancreatic ca. CAPAN2	52.9
Renal ca. UO-31	29.3	Pancreas Pool	65.1

Table BID. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3330, Run 165725930	Tissue Name	Rel. Exp.(%) Ag3330, Run 165725930
Secondary Th1 act	20.2	HUVEC IL-1beta	20.4
Secondary Th2 act	27.0	HUVEC IFN gamma	23.0
Secondary Tr1 act	41.8	HUVEC TNF alpha + IFN gamma	14.7
Secondary Th1 rest	33.4	HUVEC TNF alpha + IL4	13.7
Secondary Th2 rest	15.8	HUVEC IL-11	13.0
Secondary Tr1 rest	17.0	Lung Microvascular EC none	18.3
Primary Th1 act	14.1	Lung Microvascular EC TNFalpha + IL-1beta	13.8
Primary Th2 act	33.2	Microvascular Dermal EC none	15.7
Primary Tr1 act	37.6	Microvascular Dermal EC TNFalpha + IL-1beta	37.9
Primary Th1 rest	100.0	Bronchial epithelium TNFalpha + IL1beta	8.5
Primary Th2 rest	37.4	Small airway epithelium none	4.9
Primary Tr1 rest	34.9	Small airway epithelium TNFalpha + IL-1beta	41.5
CD45RA CD4 lymphocyte act	16.0	Coronary artery SMC rest	11.7
CD45RO CD4 lymphocyte act	28.9	Coronary artery SMC TNFalpha + IL-1beta	4.5
CD8 lymphocyte act	25.5	Astrocytes rest	33.9
Secondary CD8 lymphocyte rest	29.3	Astrocytes TNFalpha + IL-1beta	32.1
Secondary CD8 lymphocyte act	22.7	KU-812 (Basophil) rest	17.1
CD4 lymphocyte none	21.2	KU-812 (Basophil) PMA/ionomycin	44.8
2ry Th1/Th2/Tr1_anti-CD95 CH11	33.2	CCD1 106 (Keratinocytes) none	13.8
LAK cells rest	16.5	CCD1 106 (Keratinocytes) TNFalpha + IL-1beta	55.9
LAK cells IL-2	48.6	Liver cirrhosis	76.8
LAK cells IL-2+IL-12	33.2	Lupus kidney	67.8
LAK cells IL-2+IFN gamma	42.6	NCI-H292 none	39.2
LAK cells IL-2+ IL-18	30.8	NCI-H292 IL-4	57.4
LAK cells PMA/ionomycin	23.2	NCI-H292 IL-9	53.2
NK Cells IL-2 rest	20.7	NCI-H292 IL-13	23.2
Two Way MLR 3 day	41.8	NCI-H292 IFN gamma	22.8
Two Way MLR 5 day	16.0	HPAEC none	11.9
Two Way MLR 7 day	26.6	HPAEC TNF alpha + IL-1 beta	26.1
PBMC rest	16.2	Lung fibroblast none	19.6
PBMC PWM	33.0	Lung fibroblast TNF alpha + IL-1 beta	19.8
PBMC PHA-L	38.2	Lung fibroblast IL-4	13.6
Ramos (B cell) none	42.6	Lung fibroblast IL-9	15.5

Ramos (B cell) ionomycin	25.5	Lung fibroblast IL-13	14.5
B lymphocytes PWM	32.1	Lung fibroblast IFN gamma	25.5
B lymphocytes CD40L and IL-4	36.9	Dermal fibroblast CCD1070 rest	32.1
EOL-1 dbcAMP	20.2	Dermal fibroblast CCD1070 TNF alpha	62.4
EOL-1 dbcAMP PMA/ionomycin	65.1	Dermal fibroblast CCD1070 IL-1 beta	12.0
Dendritic cells none	17.4	Dermal fibroblast IFN gamma	7.2
Dendritic cells LPS	20.9	Dermal fibroblast IL-4	22.7
Dendritic cells anti-CD40	22.2	IBD Colitis 2	12.0
Monocytes rest	33.0	IBD Crohn's	11.4
Monocytes LPS	30.1	Colon	95.9
Macrophages rest	19.3	Lung	18.3
Macrophages LPS	14.8	Thymus	73.2
HUVEC none	19.5	Kidney	67.4
HUVEC starved	35.4		

AI_comprehensive_panel_v1.0 Summary: Ag3330 Expression of the CG57783-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

CNS_neurodegeneration_v1.0 Summary: Ag3330 This panel confirms the expression of the CG57783-01 gene at low levels in the brains of an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment.

General_screening_panel_v1.4 Summary: Ag3330 The CG57783-01 gene encodes a protein with homology to LINE-1 reverse transcriptase. Its expression is moderate to high across all of the samples on this panel. Therefore, this gene may be playing an important role in cellular function.

Panel 4D Summary: Ag3330 The CG57783-01 gene is expressed at high to moderate levels in a wide range of cell types of significance in the immune response in health and disease. These cells include members of the T-cell, B-cell, endothelial cell, macrophage/monocyte, and peripheral blood mononuclear cell family, as well as epithelial and fibroblast cell types from lung and skin, and normal tissues represented by colon, lung, thymus and kidney. This ubiquitous pattern of expression suggests that this gene product may be involved in homeostatic processes for these and other cell types and tissues.

This pattern is in agreement with the expression profile in General_screening_panel_v1.4 and also suggests a role for the gene product in cell survival and proliferation.

Therefore, modulation of the gene product with a functional therapeutic may lead to the alteration of functions associated with these cell types and lead to improvement of the symptoms of patients suffering from autoimmune and inflammatory diseases such as asthma, allergies, inflammatory bowel disease, lupus erythematosus, psoriasis, rheumatoid arthritis, and osteoarthritis.

NOV67

Expression of NOV67A/CG57823-01 and NOV67B/CG57823-02 was assessed using the primer-probe sets Ag3514 and Ag4117, described in Tables BJA and BJB. Results of the RTQ-PCR runs are shown in Tables BJC, BJD, and BJE. Please note that Ag3514 only recognizes the CG57823-01 variant. In addition, CG57823-02 represents a full-length physical clone of the CG57823-01 gene, validating the prediction of the gene sequence.

Table BJA. Probe Name Ag3514

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-cctcgtctcgagacaagga-3'	19	253	452
Probe	TET-5'-accatcctcgacacactccgggag-3'-TAMRA	24	274	453
Reverse	5'-cggtccttagtgggttgac-3'	20	319	454

Table BJB. Probe Name Ag4117

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ccggtacaccaatgatctgt-3'	20	342	455
Probe	TET-5'-cgaacatgctctgctgcgtcct-3'-TAMRA	23	383	456
Reverse	5'-tgacgactttccacacaa-3'	19	406	457

Table BJC. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3514, Run 210499746	Rel. Exp.(%) Ag4117, Run 206943850	Tissue Name	Rel. Exp.(%) Ag3514, Run 210499746	Rel. Exp.(%) Ag4117, Run 206943850
AD 1 Hippo	35.1	65.5	Control (Path) 3 Temporal Ctx	0.0	42.6
AD 2 Hippo	13.7	70.2	Control (Path) 4 Temporal Ctx	28.3	37.1
AD 3 Hippo	0.0	27.9	AD 1 Occipital Ctx	0.0	81.2
AD 4 Hippo	0.0	75.3	AD 2 Occipital Ctx (Missing)	0.0	73.2
AD 5 Hippo	80.1	65.1	AD 3 Occipital Ctx	0.0	71.2
AD 6 Hippo	0.0	67.4	AD 4 Occipital Ctx	75.3	50.0

Control 2 Hippo	0.0	76.8	AD 5 Occipital Ctx	12.9	66.4
Control 4 Hippo	0.0	65.5	AD 6 Occipital Ctx	0.0	45.4
Control (Path) 3 Hippo	0.0	48.3	Control 1 Occipital Ctx	15.1	74.2
AD 1 Temporal Ctx	72.2	49.3	Control 2 Occipital Ctx	0.0	69.3
AD 2 Temporal Ctx	0.0	83.5	Control 3 Occipital Ctx	0.0	38.7
AD 3 Temporal Ctx	0.0	46.7	Control 4 Occipital Ctx	41.8	83.5
AD 4 Temporal Ctx	0.0	31.6	Control (Path) 1 Occipital Ctx	14.0	72.7
AD 5 Inf Temporal Ctx	40.9	64.6	Control (Path) 2 Occipital Ctx	23.8	79.0
AD 5 Sup Temporal Ctx	0.0	23.5	Control (Path) 3 Occipital Ctx	0.0	73.2
AD 6 Inf Temporal Ctx	0.0	90.1	Control (Path) 4 Occipital Ctx	33.2	13.8
AD 6 Sup Temporal Ctx	0.0	51.4	Control 1 Parietal Ctx	0.0	39.5
Control 1 Temporal Ctx	13.8	63.7	Control 2 Parietal Ctx	0.0	64.2
Control 2 Temporal Ctx	0.0	73.7	Control 3 Parietal Ctx	0.0	51.1
Control 3 Temporal Ctx	100.0	29.7	Control (Path) 1 Parietal Ctx	50.3	16.8
Control 3 Temporal Ctx	0.0	84.7	Control (Path) 2 Parietal Ctx	0.0	25.7
Control (Path) 1 Temporal Ctx	0.0	51.1	Control (Path) 3 Parietal Ctx	0.0	100.0
Control (Path) 2 Temporal Ctx	26.2	41.2	Control (Path) 4 Parietal Ctx	0.0	37.1

Table BJD. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3514, Run 216607683	Rel. Exp.(%) Ag3514, Run 222691301	Tissue Name	Rel. Exp.(%) Ag3514, Run 216607683	Rel. Exp.(%) Ag3514, Run 222691301
Adipose	0.0	0.0	Renal ca. TK-10	0.0	0.0
Melanoma* Hs688(A).T	0.0	0.0	Bladder	35.6	0.0
Melanoma* Hs688(B).T	0.0	0.0	Gastric ca. (liver met.) NCI-N87	0.0	0.0

Melanoma* M14	0.0	0.0	Gastric ca. KATO III	0.0	0.0
Melanoma* LOXIMVI	0.0	0.0	Colon ca. SW-948	2.9	0.0
Melanoma* SK- MEL-5	0.0	0.0	Colon ca. SW480	0.0	0.0
Squamous cell carcinoma SCC-4	0.0	0.0	Colon ca.* (SW480 met) SW620	3.6	0.0
Testis Pool	0.0	0.0	Colon ca. HT29	0.0	0.0
Prostate ca.* (bone met) PC-3	0.0	0.0	Colon ca. HCT-116	0.0	0.0
Prostate Pool	0.0	0.0	Colon ca. CaCo-2	2.8	0.0
Placenta	2.3	0.0	Colon cancer tissue	0.0	0.0
Uterus Pool	0.0	0.0	Colon ca. SW1116	0.0	0.0
Ovarian ca. OVCAR-3	0.0	0.0	Colon ca. Colo-205	1.8	0.0
Ovarian ca. SK- OV-3	0.0	0.0	Colon ca. SW-48	0.0	0.0
Ovarian ca. OVCAR-4	0.0	0.0	Colon Pool	0.0	0.0
Ovarian ca. OVCAR-5	0.0	0.0	Small Intestine Pool	3.6	0.0
Ovarian ca. IGROV-1	0.0	0.0	Stomach Pool	7.2	0.0
Ovarian ca. OVCAR-8	0.0	0.0	Bone Marrow Pool	100.0	0.0
Ovary	0.0	0.0	Fetal Heart	5.7	0.0
Breast ca. MCF-7	0.0	0.0	Heart Pool	0.0	0.0
Breast ca. MDA- MB-231	2.5	0.0	Lymph Node Pool	0.0	0.0
Breast ca. BT 549	0.0	0.0	Fetal Skeletal Muscle	21.8	0.0
Breast ca. T47D	0.0	0.0	Skeletal Muscle Pool	15.1	0.0
Breast ca. MDA- N	0.0	0.0	Spleen Pool	2.2	0.0
Breast Pool	0.0	0.0	Thymus Pool	0.0	0.0
Trachea	0.0	0.0	CNS cancer (glio/astro) U87-MG	0.0	0.0
Lung	0.0	0.0	CNS cancer (glio/astro) U-118- MG	3.0	0.0
Fetal Lung	0.0	0.0	CNS cancer (neuro;met) SK-N-	0.0	0.0

			AS		
Lung ca. NCI-N417	0.0	0.0	CNS cancer (astro) SF-539	0.0	0.0
Lung ca. LX-1	3.6	0.0	CNS cancer (astro) SNB-75	20.3	0.0
Lung ca. NCI-H146	7.4	0.0	CNS cancer (glio) SNB-19	39.5	0.0
Lung ca. SHP-77	2.4	0.0	CNS cancer (glio) SF-295	0.0	0.0
Lung ca. A549	1.8	0.0	Brain (Amygdala) Pool	0.0	0.0
Lung ca. NCI-H526	0.0	0.0	Brain (cerebellum)	0.0	0.0
Lung ca. NCI-H23	0.0	0.0	Brain (fetal)	0.0	0.0
Lung ca. NCI-H460	0.0	0.0	Brain (Hippocampus) Pool	3.2	0.0
Lung ca. HOP-62	0.0	100.0	Cerebral Cortex Pool	0.0	0.0
Lung ca. NCI-H522	0.0	0.0	Brain (Substantia nigra) Pool	0.0	0.0
Liver	0.0	0.0	Brain (Thalamus) Pool	2.3	0.0
Fetal Liver	2.2	0.0	Brain (whole)	12.9	0.0
Liver ca. HepG2	0.0	0.0	Spinal Cord Pool	0.0	0.0
Kidney Pool	0.0	0.0	Adrenal Gland	0.0	0.0
Fetal Kidney	10.4	0.0	Pituitary gland Pool	0.0	0.0
Renal ca. 786-0	0.0	0.0	Salivary Gland	7.2	0.0
Renal ca. A498	0.0	0.0	Thyroid (female)	3.5	0.0
Renal ca. ACHN	0.0	0.0	Pancreatic ca. CAPAN2	0.0	0.0
Renal ca. UO-31	0.0	0.0	Pancreas Pool	0.0	0.0

Table BJE. Panel 4.1D

Tissue Name	Rel. Exp.(%) Ag4117, Run 172774997	Tissue Name	Rel. Exp.(%) Ag4117, Run 172774997
Secondary Th1 act	19.9	HUVEC IL-1beta	10.6
Secondary Th2 act	32.5	HUVEC IFN gamma	100.0
Secondary Tr1 act	31.0	HUVEC TNF alpha + IFN gamma	13.1
Secondary Th1 rest	17.7	HUVEC TNF alpha + IL4	21.3
Secondary Th2 rest	22.4	HUVEC IL-11	11.7
Secondary Tr1 rest	19.6	Lung Microvascular EC none	19.6

Primary Th1 act	26.6	Lung Microvascular EC TNFalpha + IL-1beta	35.6
Primary Th2 act	33.2	Microvascular Dermal EC none	19.6
Primary Tr1 act	27.4	Microvascular Dermal EC TNFalpha + IL-1beta	32.8
Primary Th1 rest	23.5	Bronchial epithelium TNFalpha + IL1beta	22.5
Primary Th2 rest	22.5	Small airway epithelium none	23.0
Primary Tr1 rest	25.0	Small airway epithelium TNFalpha + IL-1beta	14.0
CD45RA CD4 lymphocyte act	34.2	Coronary artery SMC rest	21.6
CD45RO CD4 lymphocyte act	39.2	Coronary artery SMC TNFalpha + IL-1beta	18.6
CD8 lymphocyte act	43.2	Astrocytes rest	31.9
Secondary CD8 lymphocyte rest	27.0	Astrocytes TNFalpha + IL-1beta	27.4
Secondary CD8 lymphocyte act	27.5	KU-812 (Basophil) rest	30.6
CD4 lymphocyte none	22.1	KU-812 (Basophil) PMA/ionomycin	33.2
2ry Th1/Th2/Tr1_anti-CD95 CH11	30.8	CCD1106 (Keratinocytes) none	13.8
LAK cells rest	38.7	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	16.8
LAK cells IL-2	33.4	Liver cirrhosis	22.4
LAK cells IL-2+IL-12	25.7	NCI-H292 none	23.2
LAK cells IL-2+IFN gamma	20.4	NCI-H292 IL-4	29.9
LAK cells IL-2+ IL-18	27.2	NCI-H292 IL-9	14.9
LAK cells PMA/ionomycin	19.8	NCI-H292 IL-13	33.0
NK Cells IL-2 rest	36.3	NCI-H292 IFN gamma	14.7
Two Way MLR 3 day	28.7	HPAEC none	20.6
Two Way MLR 5 day	16.8	HPAEC TNF alpha + IL-1 beta	24.0
Two Way MLR 7 day	9.1	Lung fibroblast none	24.0
PBMC rest	28.5	Lung fibroblast TNF alpha + IL-1 beta	26.8
PBMC PWM	22.4	Lung fibroblast IL-4	20.0
PBMC PHA-L	17.2	Lung fibroblast IL-9	22.4
Ramos (B cell) none	32.3	Lung fibroblast IL-13	23.5
Ramos (B cell) ionomycin	22.2	Lung fibroblast IFN gamma	23.7

alteration of functions associated with these cell types and lead to improvement of the symptoms of patients suffering from autoimmune and inflammatory diseases such as asthma, allergies, inflammatory bowel disease, lupus erythematosus, psoriasis, rheumatoid arthritis, and osteoarthritis.

5 **Panel 4D Summary:** Ag3514 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV68

Expression of NOV68/CG57801-01 was assessed using the primer-probe sets Ag3335 and Ag3336, described in Tables BKA and BKB. Results of the RTQ-PCR runs are shown in
10 Tables BKC, BKD, BKE and BKF.

Table BKA. Probe Name Ag3335

Primers	Sequences	Length	Start Position	Seq id no:
Forward	5'-ttgccatctattccgagtactg-3'	22	477	458
Probe	TET-5'-ccaacctcatgaagcagggaagt-3'-TAMRA	24	531	459
Reverse	5'-caggcttcaagaatgtctgt-3'	22	555	460

Table BKB. Probe Name Ag3336

Primers	Sequences	Length	Start Position	Seq id no:
Forward	5'-gtgcaagaggacaaggagatg-3'	21	1181	461
Probe	TET-5'-tcagaaaaccagaagaactgccca-3'-TAMRA	26	1213	462
Reverse	5'-cctgccttttgagcatttaac-3'	21	1240	463

Table BKC. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3335, Run 210138107	Rel. Exp.(%) Ag3335, Run 230512529	Rel. Exp.(%) Ag3336, Run 210138110	Tissue Name	Rel. Exp.(%) Ag3335, Run 210138107	Rel. Exp.(%) Ag3335, Run 230512529	Rel. Exp.(%) Ag3336, Run 210138110
AD 1 Hippo	26.1	22.8	28.1	Control (Path) 3 Temporal Ctx	5.3	4.3	6.1
AD 2 Hippo	29.9	31.9	29.5	Control (Path) 4 Temporal Ctx	18.3	15.8	17.3
AD 3 Hippo	13.7	11.8	11.7	AD 1 Occipital Ctx	11.7	12.1	15.6
AD 4 Hippo	13.4	8.3	10.4	AD 2 Occipital Ctx (Missing)	0.0	0.0	0.0
AD 5 Hippo	39.8	39.0	30.8	AD 3 Occipital Ctx	11.6	8.5	7.9
AD 6 Hippo	100.0	99.3	100.0	AD 4 Occipital Ctx	25.5	15.1	12.1
Control 2	40.3	27.4	44.8	AD 5	25.5	26.8	27.4

Hippo				Occipital Ctx			
Control 4 Hippo	26.1	25.0	27.7	AD 6 Occipital Ctx	27.4	22.2	27.9
Control (Path) 3 Hippo	15.9	7.3	12.8	Control 1 Occipital Ctx	4.9	4.6	5.8
AD 1 Temporal Ctx	28.1	24.7	33.2	Control 2 Occipital Ctx	31.6	26.8	43.2
AD 2 Temporal Ctx	26.8	21.9	23.5	Control 3 Occipital Ctx	13.7	13.8	6.0
AD 3 Temporal Ctx	6.2	8.3	6.7	Control 4 Occipital Ctx	11.7	11.7	11.6
AD 4 Temporal Ctx	27.5	22.4	21.9	Control (Path) 1 Occipital Ctx	50.7	48.0	48.0
AD 5 Inf Temporal Ctx	84.1	80.7	63.7	Control (Path) 2 Occipital Ctx	13.2	7.9	7.8
AD 5 Sup Temporal Ctx	52.9	58.6	52.9	Control (Path) 3 Occipital Ctx	4.0	4.2	3.9
AD 6 Inf Temporal Ctx	95.9	100.0	97.3	Control (Path) 4 Occipital Ctx	11.0	11.3	10.8
AD 6 Sup Temporal Ctx	67.4	67.4	54.3	Control 1 Parietal Ctx	11.8	7.3	9.9
Control 1 Temporal Ctx	8.4	6.8	8.0	Control 2 Parietal Ctx	48.6	37.6	49.7
Control 2 Temporal Ctx	25.2	31.0	25.0	Control 3 Parietal Ctx	22.7	12.8	13.6
Control 3 Temporal Ctx	15.9	16.3	13.5	Control (Path) 1 Parietal Ctx	27.0	24.7	28.1
Control 3 Temporal Ctx	12.1	8.1	9.4	Control (Path) 2 Parietal Ctx	19.8	16.7	16.3
Control (Path) 1 Temporal Ctx	26.2	27.5	30.6	Control (Path) 3 Parietal Ctx	4.0	3.8	0.4
Control (Path) 2 Temporal Ctx	19.5	20.6	13.3	Control (Path) 4 Parietal Ctx	27.4	23.7	25.2

Table BKD. General screening panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3335, Run 213333209	Rel. Exp.(%) Ag3336, Run 215773745	Tissue Name	Rel. Exp.(%) Ag3335, Run 213333209	Rel. Exp.(%) Ag3336, Run 215773745
Adipose	4.0	4.6	Renal ca. TK-10	12.2	12.2

Melanoma* Hs688(A).T	2.5	2.0	Bladder	24.0	19.8
Melanoma* Hs688(B).T	0.8	0.7	Gastric ca. (liver met.) NCI-N87	29.5	21.6
Melanoma* M14	30.1	28.9	Gastric ca. KATO III	52.5	41.2
Melanoma* LOXIMVI	2.4	2.4	Colon ca. SW-948	4.3	6.2
Melanoma* SK- MEL-5	7.5	12.0	Colon ca. SW480	100.0	100.0
Squamous cell carcinoma SCC-4	1.9	1.8	Colon ca.* (SW480 met) SW620	49.3	57.4
Testis Pool	5.1	4.1	Colon ca. HT29	12.7	13.4
Prostate ca.* (bone met) PC-3	9.6	7.3	Colon ca. HCT-116	14.2	16.7
Prostate Pool	11.4	9.3	Colon ca. CaCo-2	13.2	9.9
Placenta	13.9	9.5	Colon cancer tissue	20.3	23.5
Uterus Pool	2.9	2.1	Colon ca. SW1116	5.6	7.5
Ovarian ca. OVCAR-3	6.4	4.9	Colon ca. Colo-205	32.1	39.2
Ovarian ca. SK- OV-3	12.5	12.5	Colon ca. SW-48	10.9	10.6
Ovarian ca. OVCAR-4	2.6	2.0	Colon Pool	6.9	5.2
Ovarian ca. OVCAR-5	15.1	15.3	Small Intestine Pool	6.1	6.5
Ovarian ca. IGROV-1	7.5	6.6	Stomach Pool	7.6	4.1
Ovarian ca. OVCAR-8	2.5	2.6	Bone Marrow Pool	2.0	2.5
Ovary	9.5	8.4	Fetal Heart	3.3	1.7
Breast ca. MCF-7	27.9	20.6	Heart Pool	3.0	4.8
Breast ca. MDA- MB-231	5.7	6.2	Lymph Node Pool	4.9	5.7
Breast ca. BT 549	3.8	3.5	Fetal Skeletal Muscle	0.8	0.7
Breast ca. T47D	23.2	32.1	Skeletal Muscle Pool	1.9	1.4
Breast ca. MDA- N	9.6	9.8	Spleen Pool	49.0	39.0
Breast Pool	6.9	5.6	Thymus Pool	9.6	0.0
Trachea	10.6	6.5	CNS cancer (glio/astro) U87-MG	2.1	3.2
Lung	2.8	2.9	CNS cancer (glio/astro) U-118- MG	6.7	4.4
Fetal Lung	11.3	10.5	CNS cancer (neuro;met) SK-N- AS	0.6	0.2
Lung ca. NCI- N417	2.6	2.9	CNS cancer (astro) SF-539	1.4	1.5
Lung ca. LX-1	79.0	92.0	CNS cancer (astro) SNB-75	6.6	11.3
Lung ca. NCI- H146	2.0	2.7	CNS cancer (glio) SNB-19	5.8	7.3
Lung ca. SHP-77	0.0	0.0	CNS cancer (glio) SF-295	29.7	18.0
Lung ca. A549	5.0	5.4	Brain (Amygdala) Pool	14.9	9.0
Lung ca. NCI- H526	2.4	3.2	Brain (cerebellum)	7.7	6.9
Lung ca. NCI-H23	2.3	2.4	Brain (fetal)	10.2	7.6

Lung ca. NCI-H460	1.8	2.4	Brain (Hippocampus) Pool	13.6	9.5
Lung ca. HOP-62	1.7	1.2	Cerebral Cortex Pool	12.6	7.6
Lung ca. NCI-H522	1.1	0.8	Brain (Substantia nigra) Pool	14.9	9.5
Liver	1.6	1.0	Brain (Thalamus) Pool	19.5	12.3
Fetal Liver	6.3	15.2	Brain (whole)	9.0	7.2
Liver ca. HepG2	7.6	7.7	Spinal Cord Pool	21.0	16.2
Kidney Pool	10.6	8.5	Adrenal Gland	12.3	7.2
Fetal Kidney	11.0	10.6	Pituitary gland Pool	2.9	1.8
Renal ca. 786-0	7.1	7.7	Salivary Gland	3.1	3.0
Renal ca. A498	1.8	2.9	Thyroid (female)	5.0	4.9
Renal ca. ACHN	4.0	3.4	Pancreatic ca. CAPAN2	14.0	12.6
Renal ca. UO-31	1.9	2.0	Pancreas Pool	13.4	11.9

Table BKE. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag3335, Run 173762744	Tissue Name	Rel. Exp.(%) Ag3335, Run 173762744
Normal Colon	12.8	Kidney Margin (OD04348)	100.0
Colon cancer (OD06064)	12.2	Kidney malignant cancer (OD06204B)	5.7
Colon Margin (OD06064)	8.1	Kidney normal adjacent tissue (OD06204E)	9.7
Colon cancer (OD06159)	1.6	Kidney Cancer (OD04450-01)	35.4
Colon Margin (OD06159)	10.6	Kidney Margin (OD04450-03)	25.5
Colon cancer (OD06297-04)	3.8	Kidney Cancer 8120613	1.8
Colon Margin (OD06297-05)	11.4	Kidney Margin 8120614	10.7
CC Gr.2 ascend colon (ODO3921)	8.0	Kidney Cancer 9010320	1.8
CC Margin (ODO3921)	3.1	Kidney Margin 9010321	6.7
Colon cancer metastasis (OD06104)	6.6	Kidney Cancer 8120607	6.1
Lung Margin (OD06104)	4.5	Kidney Margin 8120608	3.5
Colon mets to lung (OD04451-01)	4.8	Normal Uterus	4.3
Lung Margin (OD04451-02)	21.3	Uterine Cancer 064011	6.6
Normal Prostate	5.8	Normal Thyroid	1.7
Prostate Cancer (OD04410)	11.5	Thyroid Cancer 064010	3.4
Prostate Margin (OD04410)	9.5	Thyroid Cancer A302152	9.7
Normal Ovary	11.0	Thyroid Margin A302153	6.6
Ovarian cancer (OD06283-03)	7.3	Normal Breast	15.2
Ovarian Margin (OD06283-07)	6.5	Breast Cancer (OD04566)	3.2
Ovarian Cancer 064008	6.6	Breast Cancer 1024	12.1
Ovarian cancer (OD06145)	10.3	Breast Cancer (OD04590-01)	5.8
Ovarian Margin (OD06145)	12.4	Breast Cancer Mets (OD04590-03)	9.6
Ovarian cancer (OD06455-03)	5.8	Breast Cancer Metastasis (OD04655-05)	22.8
Ovarian Margin (OD06455-07)	1.7	Breast Cancer 064006	14.1
Normal Lung	13.1	Breast Cancer 9100266	16.7
Invasive poor diff. lung adeno (ODO4945-01)	6.7	Breast Margin 9100265	7.6
Lung Margin (ODO4945-03)	24.1	Breast Cancer A209073	4.6
Lung Malignant Cancer	12.8	Breast Margin A2090734	15.8

(OD03126)			
Lung Margin (OD03126)	5.4	Breast cancer (OD06083)	12.4
Lung Cancer (OD05014A)	11.6	Breast cancer node metastasis (OD06083)	12.8
Lung Margin (OD05014B)	16.4	Normal Liver	16.7
Lung cancer (OD06081)	2.0	Liver Cancer 1026	2.0
Lung Margin (OD06081)	10.2	Liver Cancer 1025	13.6
Lung Cancer (OD04237-01)	5.9	Liver Cancer 6004-T	11.8
Lung Margin (OD04237-02)	21.8	Liver Tissue 6004-N	6.7
Ocular Melanoma Metastasis	1.2	Liver Cancer 6005-T	9.7
Ocular Melanoma Margin (Liver)	7.4	Liver Tissue 6005-N	13.5
Melanoma Metastasis	16.8	Liver Cancer 064003	16.6
Melanoma Margin (Lung)	24.7	Normal Bladder	14.1
Normal Kidney	9.3	Bladder Cancer 1023	9.1
Kidney Ca, Nuclear grade 2 (OD04338)	45.1	Bladder Cancer A302173	4.5
Kidney Margin (OD04338)	9.5	Normal Stomach	33.0
Kidney Ca Nuclear grade 1/2 (OD04339)	72.2	Gastric Cancer 9060397	2.6
Kidney Margin (OD04339)	18.7	Stomach Margin 9060396	11.3
Kidney Ca, Clear cell type (OD04340)	7.2	Gastric Cancer 9060395	8.7
Kidney Margin (OD04340)	18.3	Stomach Margin 9060394	11.4
Kidney Ca, Nuclear grade 3 (OD04348)	2.8	Gastric Cancer 064005	18.3

Table BKF. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3335, Run 165128064	Rel. Exp.(%) Ag3336, Run 165128065	Tissue Name	Rel. Exp.(%) Ag3335, Run 165128064	Rel. Exp.(%) Ag3336, Run 165128065
Secondary Th1 act	32.1	14.0	HUVEC IL-1beta	2.7	0.4
Secondary Th2 act	42.6	14.6	HUVEC IFN gamma	3.3	0.8
Secondary Tr1 act	43.5	11.6	HUVEC TNF alpha + IFN gamma	5.8	0.8
Secondary Th1 rest	9.0	3.1	HUVEC TNF alpha + IL4	7.5	1.7
Secondary Th2 rest	15.5	4.0	HUVEC IL-11	1.6	0.5
Secondary Tr1 rest	15.4	3.3	Lung Microvascular EC none	2.7	0.4
Primary Th1 act	38.2	9.3	Lung Microvascular EC TNFalpha + IL-1beta	1.7	0.4
Primary Th2 act	34.4	8.1	Microvascular Dermal EC none	2.8	0.7
Primary Tr1 act	40.6	0.2	Microvascular Dermal EC TNFalpha + IL-1beta	2.5	0.6
Primary Th1 rest	62.4	15.5	Bronchial epithelium TNFalpha + IL1beta	0.5	0.2
Primary Th2 rest	41.8	100.0	Small airway epithelium none	0.8	0.2
Primary Tr1 rest	29.3	6.3	Small airway epithelium TNFalpha + IL-1beta	2.6	0.3
CD45RA CD4 lymphocyte act	20.4	5.3	Coronary artery SMC rest	5.4	1.2
CD45RO CD4 lymphocyte act	45.7	11.0	Coronary artery SMC TNFalpha + IL-1beta	3.4	0.8
CD8 lymphocyte act	41.8	7.7	Astrocytes rest	3.5	0.8

Secondary CD8 lymphocyte rest	42.3	6.4	Astrocytes TNFalpha + IL-1beta	6.4	1.5
Secondary CD8 lymphocyte act	28.5	5.0	KU-812 (Basophil) rest	6.3	1.0
CD4 lymphocyte none	23.5	3.4	KU-812 (Basophil) PMA/ionomycin	19.9	4.5
2ry Th1/Th2/Tr1_anti-CD95 CH11	29.7	6.2	CCD1106 (Keratinocytes) none	1.2	0.2
LAK cells rest	39.0	6.9	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.1	0.1
LAK cells IL-2	58.2	12.8	Liver cirrhosis	5.7	1.2
LAK cells IL-2+IL-12	47.0	7.2	Lupus kidney	3.0	0.9
LAK cells IL-2+IFN gamma	66.4	10.5	NCI-H292 none	3.8	0.8
LAK cells IL-2+ IL-18	49.7	7.8	NCI-H292 IL-4	5.0	0.6
LAK cells PMA/ionomycin	20.3	4.5	NCI-H292 IL-9	5.1	2.6
NK Cells IL-2 rest	47.3	9.7	NCI-H292 IL-13	3.2	0.4
Two Way MLR 3 day	49.3	9.7	NCI-H292 IFN gamma	1.6	0.5
Two Way MLR 5 day	28.1	6.7	HPAEC none	1.7	0.2
Two Way MLR 7 day	26.6	5.8	HPAEC TNF alpha + IL-1 beta	3.4	0.8
PBMC rest	22.1	3.3	Lung fibroblast none	6.7	2.1
PBMC PWM	100.0	25.0	Lung fibroblast TNF alpha + IL-1 beta	6.4	2.0
PBMC PHA-L	41.8	8.0	Lung fibroblast IL-4	45.7	13.4
Ramos (B cell) none	4.3	0.7	Lung fibroblast IL-9	17.2	2.1
Ramos (B cell) ionomycin	17.9	2.4	Lung fibroblast IL-13	32.8	8.8
B lymphocytes PWM	79.6	11.0	Lung fibroblast IFN gamma	51.8	9.9
B lymphocytes CD40L and IL-4	22.2	3.9	Dermal fibroblast CCD1070 rest	7.3	1.8
EOL-1 dbcAMP	1.8	0.4	Dermal fibroblast CCD1070 TNF alpha	42.9	13.4
EOL-1 dbcAMP PMA/ionomycin	13.0	2.4	Dermal fibroblast CCD1070 IL-1 beta	8.4	2.3
Dendritic cells none	13.2	1.8	Dermal fibroblast IFN gamma	9.0	2.8
Dendritic cells LPS	21.0	4.0	Dermal fibroblast IL-4	12.4	3.5
Dendritic cells anti-CD40	8.7	1.9	IBD Colitis 2	1.7	0.4
Monocytes rest	16.2	2.4	IBD Crohn's	3.2	0.8
Monocytes LPS	12.8	3.8	Colon	17.7	4.5
Macrophages rest	37.6	7.2	Lung	10.6	2.8
Macrophages LPS	21.5	3.0	Thymus	35.1	13.7
HUVEC none	4.5	0.9	Kidney	27.2	8.6
HUVEC starved	12.0	1.6			

CNS_neurodegeneration_v1.0 Summary: Ag3335/Ag3336 Results from three experiments using two different probe/primer sets are in excellent agreement and when analyzed by ANCOVA p = 0.01 and p = 0.01. This panel confirms the expression of the CG57801-01 gene at moderate levels in the brains of an independent group of individuals.

This gene is found to be upregulated in the temporal cortex of Alzheimer's disease patients. The CG57801-01 gene encodes a protein with homology to guanine nucleotide exchange factor. Inhibition of the CG57801-01 gene or its protein product may decrease neuronal death and be of use in the treatment of Alzheimer's disease.

5 **General_screening_panel_v1.4 Summary:** Ag3335/Ag3336 Results from two experiments using two different probe/primer sets are in excellent agreement. Expression of the CG57801-01 gene appears to be upregulated in a number of colon cancer cell lines, when compared to normal colon. Therefore, expression of this gene may be used to distinguish colon cancer cell lines from the other samples on this panel. Furthermore, therapeutic
10 modulation of the activity of this gene or its protein product, using small molecule drugs, antibodies, and protein therapeutics, may be of use in the treatment of colon cancer. These results are consistent with what is observed in Panel 2.2. The CG57801-01 gene encodes a putative guanine nucleotide exchange factor (GEF) that is homologous to the ASEF protein. ASEF is known to stimulate cell flattening, membrane ruffling, and lamellipodia formation in
15 the presence of APC (adenomatous polyposis coli protein), suggesting that the APC-Asef complex may regulate the actin cytoskeletal network, cell morphology and migration, and neuronal function (ref. 1). The adenomatous polyposis coli gene (APC) is mutated in familial adenomatous polyposis and in sporadic colorectal tumors.

In addition, this gene is expressed at high levels in all regions of the central nervous
20 system examined, including amygdala, hippocampus, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord. Therefore, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression. The CG57801-01 gene also displays significant homology to the collybistin gene. Collybistin is a newly identified brain-specific GEF that induces
25 submembrane clustering of gephyrin and may be an important determinant of inhibitory postsynaptic membrane formation and plasticity (ref. 2).

Among tissues with metabolic or endocrine function, this gene is expressed at high to moderate levels in pancreas, adipose, adrenal gland, thyroid, pituitary gland, skeletal muscle, heart, liver and the gastrointestinal tract. Therefore, therapeutic modulation of the activity of
30 this gene may prove useful in the treatment of endocrine/metabolically related diseases, such as obesity and diabetes. This gene is well-expressed in pancreas, which includes the insulin-secreting beta cells in the islets of Langerhans. Guanine nucleotide exchange factors are present in beta cells and are activated by cAMP. A rise in cAMP levels precedes glucose-

induced insulin secretion (Ref. 3). Thus, the CG57801-01 gene may be a target for therapeutic modulation of the beta cell secretory defect in Type 2 diabetes.

References:

1. Kawasaki Y, Senda T, Ishidate T, Koyama R, Morishita T, Iwayama Y, Higuchi O, Akiyama T. (2000) Asef, a link between the tumor suppressor APC and G-protein signaling. Science 289(5482):1194-7

The adenomatous polyposis coli gene (APC) is mutated in familial adenomatous polyposis and in sporadic colorectal tumors. Here the APC gene product is shown to bind through its armadillo repeat domain to a Rac-specific guanine nucleotide exchange factor (GEF), termed Asef. Endogenous APC colocalized with Asef in mouse colon epithelial cells and neuronal cells. Furthermore, APC enhanced the GEF activity of Asef and stimulated Asef-mediated cell flattening, membrane ruffling, and lamellipodia formation in MDCK cells. These results suggest that the APC-Asef complex may regulate the actin cytoskeletal network, cell morphology and migration, and neuronal function.

PMID: 10947987

2. Kins S, Betz H, Kirsch J (2000) Collybistin, a newly identified brain-specific GEF, induces submembrane clustering of gephyrin. Nat Neurosci 3(1):22-9

The formation of postsynaptic GABAA and glycine receptor clusters requires the receptor-associated peripheral membrane protein gephyrin. Here we describe two splice variants of a novel gephyrin-binding protein, termed collybistin I and II, which belong to the family of dbl-like GDP/GTP exchange factors (GEFs). Co-expression of collybistin II with gephyrin induced the formation of submembrane gephyrin aggregates that accumulate hetero-oligomeric glycine receptors. Our data suggest that collybistin II regulates the membrane deposition of gephyrin by activating a GTPase of the Rho/Rac family. Therefore, this protein may be an important determinant of inhibitory postsynaptic membrane formation and plasticity.

PMID: 10607391

3. Leech CA, Holz GG, Chepurny O, Habener JF. (2000) Expression of cAMP-regulated guanine nucleotide exchange factors in pancreatic beta-cells. Biochem Biophys Res Commun. 278(1):44-7.

The insulinotropic hormone glucagon-like peptide-1 (GLP-1) binds to a Gs-coupled receptor on pancreatic beta-cells and potentiates glucose-induced insulin secretion, insulin

gene transcription, and beta-cell growth. These stimulatory effects have been attributed to the elevation of intracellular cAMP levels, though it is now apparent that some stimulatory effects of GLP-1 occur independently of the cAMP-mediated activation of protein kinase A (PKA). The nature of this alternative, PKA-independent signaling pathway remains unknown. Here we present evidence for the expression of type 1 and type 2 cAMP-regulated guanine nucleotide exchange factors (cAMP-GEFs) in beta-cells. GEFs are activated by their binding of cAMP. Because cAMP-GEFs activate Ras/MAPK proliferation signaling pathways, they may play an important role in PKA-independent, GLP-1-mediated, signaling pathways in the regulation of beta-cell growth and differentiation.

PMID: 11071853

Panel 2.2 Summary: Ag3335 The CG57801-01 gene encodes a protein with homology to APC-stimulated guanine nucleotide exchange factor (ASEF). Its expression is low to moderate in all of the samples on this panel. Interestingly, expression of this gene is lower in some colon, lung and kidney cancer tissues compared to matched normal tissues. This observation suggests that expression of this gene can be used to distinguish these cancers from normal tissues. Also, therapeutic modulation of the activity of the protein encoded by this gene may be beneficial in the treatment of colon, kidney and lung cancer.

ASEF is known to mediate cell flattening, membrane ruffling, and lamellipodia formation which is stimulated by presence of APC (adenomatous polyposis coli gene) (Ref 1). The adenomatous polyposis coli gene (APC) is mutated in familial adenomatous polyposis and in sporadic colorectal tumors.

References:

1. Kawasaki Y, Senda T, Ishidate T, Koyama R, Morishita T, Iwayama Y, Higuchi O, Akiyama T. (2000) Asef, a link between the tumor suppressor APC and G-protein signaling. Science 289(5482):1194-7

The adenomatous polyposis coli gene (APC) is mutated in familial adenomatous polyposis and in sporadic colorectal tumors. Here the APC gene product is shown to bind through its armadillo repeat domain to a Rac-specific guanine nucleotide exchange factor (GEF), termed Asef. Endogenous APC colocalized with Asef in mouse colon epithelial cells and neuronal cells. Furthermore, APC enhanced the GEF activity of Asef and stimulated Asef-mediated cell flattening, membrane ruffling, and lamellipodia formation in MDCK cells. These results suggest that the APC-Asef complex may regulate the actin cytoskeletal network, cell morphology and migration, and neuronal function.

10947987

Panel 4D Summary: Ag3336/Ag3335 The CG57801-01 transcript is expressed in several tissues. It is expressed in most lymphocytes, in both unstimulated and stimulated T cells. The expression of this gene is upregulate in B cells and PBMC treated with pokeweed mitogen. Myeloid cells also express the transcript. Most non-hematopoietic cell types do not consistently express this transcript with the exception of fibroblasts which upregulate the transcript in response to IL-4, IL-13, gamma interferon and tnfa. The expression profile of this gene suggests that it may be important in the normal function or activation of leukocytes and fibroblasts. Therefore, modulation of the gene product with a functional therapeutic may be useful for immunomodulation, or to treat diseases such as asthma, emphysema, psoriasis, and arthritis.

NOV69

Expression of NOV69/CG57719-01 was assessed using the primer-probe sets Ag3314 and Ag4358, described in Tables BLA and BLB. Results of the RTQ-PCR runs are shown in Tables BLC, BLD and BLE.

Table BLA. Probe Name Ag3314

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ggaatacctggtcaggaagaag-3'	22	1280	464
Probe	TET-5'-cacatctatatcccaagaacgggtca-3'-TAMRA	26	1302	465
Reverse	5'-ttggcattgatacagctgaagt-3'	22	1333	466

Table BLB. Probe Name Ag4358

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-tgtctcaaggctttagttctt-3'	22	901	467
Probe	TET-5'-ctgcagccagctctgtccaaa-3'-TAMRA	23	923	468
Reverse	5'-tcccactccttcataataat-3'	22	954	469

Table BLC. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3314, Run 210138296	Rel. Exp.(%) Ag4358, Run 224372540	Tissue Name	Rel. Exp.(%) Ag3314, Run 210138296	Rel. Exp.(%) Ag4358, Run 224372540
AD 1 Hippo	4.6	25.2	Control (Path) 3 Temporal Ctx	0.0	9.7
AD 2 Hippo	18.6	52.5	Control (Path) 4 Temporal Ctx	74.2	39.0
AD 3 Hippo	4.1	8.5	AD 1 Occipital Ctx	16.4	14.6
AD 4 Hippo	6.4	11.8	AD 2 Occipital Ctx (Missing)	0.0	0.0
AD 5 Hippo	35.6	51.4	AD 3 Occipital Ctx	7.4	8.2
AD 6 Hippo	61.6	95.9	AD 4 Occipital Ctx	11.7	29.7

Control 2 Hippo	5.8	29.3	AD 5 Occipital Ctx	10.7	46.3
Control 4 Hippo	5.7	36.1	AD 6 Occipital Ctx	5.4	37.4
Control (Path) 3 Hippo	0.0	9.6	Control 1 Occipital Ctx	0.0	8.4
AD 1 Temporal Ctx	4.2	25.2	Control 2 Occipital Ctx	4.3	77.9
AD 2 Temporal Ctx	14.9	43.2	Control 3 Occipital Ctx	36.6	15.3
AD 3 Temporal Ctx	0.0	5.4	Control 4 Occipital Ctx	0.0	14.8
AD 4 Temporal Ctx	11.5	25.2	Control (Path) 1 Occipital Ctx	12.4	66.4
AD 5 Inf Temporal Ctx	13.9	87.7	Control (Path) 2 Occipital Ctx	19.3	12.8
AD 5 Sup Temporal Ctx	16.6	100.0	Control (Path) 3 Occipital Ctx	0.0	9.5
AD 6 Inf Temporal Ctx	55.1	78.5	Control (Path) 4 Occipital Ctx	27.5	12.4
AD 6 Sup Temporal Ctx	100.0	80.1	Control 1 Parietal Ctx	21.5	18.9
Control 1 Temporal Ctx	15.6	13.1	Control 2 Parietal Ctx	20.0	53.6
Control 2 Temporal Ctx	24.3	42.0	Control 3 Parietal Ctx	0.0	17.0
Control 3 Temporal Ctx	19.1	12.7	Control (Path) 1 Parietal Ctx	20.6	49.0
Control 3 Temporal Ctx	0.0	14.7	Control (Path) 2 Parietal Ctx	5.8	30.6
Control (Path) 1 Temporal Ctx	15.8	58.2	Control (Path) 3 Parietal Ctx	5.8	17.0
Control (Path) 2 Temporal Ctx	8.3	33.0	Control (Path) 4 Parietal Ctx	37.6	22.4

Table BLD. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3314, Run 215678552	Tissue Name	Rel. Exp.(%) Ag3314, Run 215678552
Adipose	1.0	Renal ca. TK-10	0.0
Melanoma* Hs688(A).T	0.0	Bladder	0.0
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	0.0	Colon ca. SW-948	0.8
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	0.0
Squamous cell carcinoma SCC-4	0.0	Colon ca.* (SW480 met) SW620	0.8
Testis Pool	100.0	Colon ca. HT29	0.0
Prostate ca.* (bone met) PC-3	0.0	Colon ca. HCT-116	0.9
Prostate Pool	1.0	Colon ca. CaCo-2	0.0
Placenta	3.5	Colon cancer tissue	0.0
Uterus Pool	0.7	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	0.0	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	0.0	Colon Pool	0.0
Ovarian ca. OVCAR-5	38.2	Small Intestine Pool	9.9
Ovarian ca. IGROV-1	0.0	Stomach Pool	2.3

Ovarian ca. OVCAR-8	0.0	Bone Marrow Pool	0.8
Ovary	5.7	Fetal Heart	0.9
Breast ca. MCF-7	0.0	Heart Pool	1.7
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	0.9
Breast ca. BT 549	0.0	Fetal Skeletal Muscle	0.0
Breast ca. T47D	0.0	Skeletal Muscle Pool	0.0
Breast ca. MDA-N	0.0	Spleen Pool	0.0
Breast Pool	1.2	Thymus Pool	2.5
Trachea	1.2	CNS cancer (glio/astro) U87-MG	0.0
Lung	73.7	CNS cancer (glio/astro) U-118-MG	1.4
Fetal Lung	0.0	CNS cancer (neuro;met) SK-N-AS	0.0
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	1.2	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	0.0	CNS cancer (glio) SNB-19	1.7
Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	0.0
Lung ca. A549	0.7	Brain (Amygdala) Pool	1.7
Lung ca. NCI-H526	0.0	Brain (cerebellum)	0.0
Lung ca. NCI-H23	0.0	Brain (fetal)	0.0
Lung ca. NCI-H460	0.0	Brain (Hippocampus) Pool	5.2
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	2.1
Lung ca. NCI-H522	2.0	Brain (Substantia nigra) Pool	0.0
Liver	0.0	Brain (Thalamus) Pool	0.0
Fetal Liver	0.0	Brain (whole)	4.5
Liver ca. HepG2	0.0	Spinal Cord Pool	0.0
Kidney Pool	25.0	Adrenal Gland	0.0
Fetal Kidney	9.6	Pituitary gland Pool	0.0
Renal ca. 786-0	0.0	Salivary Gland	0.0
Renal ca. A498	0.0	Thyroid (female)	0.0
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.0	Pancreas Pool	0.0

Table BLE. General_screening_panel_v1.5

Tissue Name	Rel. Exp.(%) Ag4358, Run 244373100	Tissue Name	Rel. Exp.(%) Ag4358, Run 244373100
Adipose	0.0	Renal ca. TK-10	0.0
Melanoma* Hs688(A).T	0.0	Bladder	0.0
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	0.0	Colon ca. SW-948	2.9
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	0.0
Squamous cell carcinoma SCC-4	0.0	Colon ca. * (SW480 met) SW620	0.0
Testis Pool	100.0	Colon ca. HT29	0.0
Prostate ca. * (bone met) PC-3	0.0	Colon ca. HCT-116	0.0
Prostate Pool	0.0	Colon ca. CaCo-2	0.0
Placenta	0.0	Colon cancer tissue	0.0
Uterus Pool	0.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	0.0	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	2.1	Colon Pool	0.0

General_screening_panel_v1.5 Summary: Ag4358 Expression of the CG57719-01 gene is restricted to a sample derived from testis (CT = 32.67). This observation is consistent with the results obtained using Ag3314 on Panel 1.4. Thus, the expression of this gene could be used to distinguish testis from the other samples in the panel. Furthermore, therapeutic modulation of this gene product may be useful for the diagnosis and/or treatment of fertility and hypogonadism.

Panel 4.1D Summary: Ag4358 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 4D Summary: Ag3314 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV70

Expression of NOV70/CG57462-01 was assessed using the primer-probe set Ag3247, described in Table BMA. Results of the RTQ-PCR runs are shown in Tables BMB, BMC, BMD and BME.

Table BMA. Probe Name Ag3247

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gacgttcaacaatgacatgct-3'	21	1940	470
Probe	TET-5'-cttcatcagcagcagctgcattgct-3'-TAMRA	25	1967	471
Reverse	5'-agcaggagggtgaggatgtagac-3'	22	1998	472

Table BMB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3247, Run 210037961	Tissue Name	Rel. Exp.(%) Ag3247, Run 210037961
AD 1 Hippo	18.8	Control (Path) 3 Temporal Ctx	3.7
AD 2 Hippo	28.1	Control (Path) 4 Temporal Ctx	32.3
AD 3 Hippo	3.2	AD 1 Occipital Ctx	14.7
AD 4 Hippo	7.9	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	97.9	AD 3 Occipital Ctx	3.2
AD 6 Hippo	37.6	AD 4 Occipital Ctx	11.5
Control 2 Hippo	30.1	AD 5 Occipital Ctx	15.2
Control 4 Hippo	8.7	AD 6 Occipital Ctx	25.0
Control (Path) 3 Hippo	3.4	Control 1 Occipital Ctx	1.8
AD 1 Temporal Ctx	17.7	Control 2 Occipital Ctx	59.9
AD 2 Temporal Ctx	41.8	Control 3 Occipital Ctx	17.3
AD 3 Temporal Ctx	6.7	Control 4 Occipital Ctx	6.7
AD 4 Temporal Ctx	27.2	Control (Path) 1 Occipital Ctx	81.2
AD 5 Inf Temporal Ctx	100.0	Control (Path) 2 Occipital Ctx	10.8
AD 5 Sup Temporal Ctx	57.4	Control (Path) 3 Occipital	0.6

		Ctx	
AD 6 Inf Temporal Ctx	23.2	Control (Path) 4 Occipital Ctx	18.7
AD 6 Sup Temporal Ctx	43.5	Control 1 Parietal Ctx	7.5
Control 1 Temporal Ctx	6.0	Control 2 Parietal Ctx	57.8
Control 2 Temporal Ctx	16.3	Control 3 Parietal Ctx	14.4
Control 3 Temporal Ctx	11.7	Control (Path) 1 Parietal Ctx	37.9
Control 3 Temporal Ctx	12.4	Control (Path) 2 Parietal Ctx	26.1
Control (Path) 1 Temporal Ctx	61.6	Control (Path) 3 Parietal Ctx	2.2
Control (Path) 2 Temporal Ctx	32.1	Control (Path) 4 Parietal Ctx	29.7

Table BMC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3247, Run 214693633	Tissue Name	Rel. Exp.(%) Ag3247, Run 214693633
Adipose	0.1	Renal ca. TK-10	1.9
Melanoma* Hs688(A).T	0.1	Bladder	0.5
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	0.1	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	0.1	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	1.2
Squamous cell carcinoma SCC-4	0.5	Colon ca.* (SW480 met) SW620	1.1
Testis Pool	2.8	Colon ca. HT29	0.3
Prostate ca.* (bone met) PC-3	0.7	Colon ca. HCT-116	1.6
Prostate Pool	0.3	Colon ca. CaCo-2	0.9
Placenta	0.0	Colon cancer tissue	0.0
Uterus Pool	0.0	Colon ca. SW1116	1.2
Ovarian ca. OVCAR-3	0.3	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	0.1	Colon ca. SW-48	0.1
Ovarian ca. OVCAR-4	0.0	Colon Pool	0.2
Ovarian ca. OVCAR-5	0.4	Small Intestine Pool	0.1
Ovarian ca. IGROV-1	0.1	Stomach Pool	0.4
Ovarian ca. OVCAR-8	0.1	Bone Marrow Pool	0.0
Ovary	0.1	Fetal Heart	0.0
Breast ca. MCF-7	4.2	Heart Pool	0.0
Breast ca. MDA-MB-231	0.2	Lymph Node Pool	0.1
Breast ca. BT 549	0.4	Fetal Skeletal Muscle	0.1
Breast ca. T47D	0.9	Skeletal Muscle Pool	0.0
Breast ca. MDA-N	0.4	Spleen Pool	0.1
Breast Pool	0.4	Thymus Pool	0.6
Trachea	0.0	CNS cancer (glio/astro) U87-MG	0.0
Lung	0.1	CNS cancer (glio/astro) U-118-MG	0.0
Fetal Lung	0.5	CNS cancer (neuro;met) SK-N-AS	0.2
Lung ca. NCI-N417	8.7	CNS cancer (astro) SF-539	0.1
Lung ca. LX-1	0.2	CNS cancer (astro) SNB-75	0.2
Lung ca. NCI-H146	1.6	CNS cancer (glio) SNB-19	0.0
Lung ca. SHP-77	6.3	CNS cancer (glio) SF-295	0.4

Lung ca. A549	0.0	Brain (Amygdala) Pool	3.6
Lung ca. NCI-H526	1.2	Brain (cerebellum)	16.7
Lung ca. NCI-H23	4.5	Brain (fetal)	100.0
Lung ca. NCI-H460	0.4	Brain (Hippocampus) Pool	6.0
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	6.0
Lung ca. NCI-H522	2.2	Brain (Substantia nigra) Pool	5.6
Liver	0.0	Brain (Thalamus) Pool	6.8
Fetal Liver	0.1	Brain (whole)	12.8
Liver ca. HepG2	0.4	Spinal Cord Pool	3.8
Kidney Pool	0.0	Adrenal Gland	0.4
Fetal Kidney	1.6	Pituitary gland Pool	0.7
Renal ca. 786-0	0.7	Salivary Gland	0.0
Renal ca. A498	0.2	Thyroid (female)	0.0
Renal ca. ACHN	0.1	Pancreatic ca. CAPAN2	1.2
Renal ca. UO-31	0.5	Pancreas Pool	0.5

Table BMD. Panel 2.2

Tissue Name	Rel. Exp.(%) Ag3247, Run 174441297	Tissue Name	Rel. Exp.(%) Ag3247, Run 174441297
Normal Colon	0.7	Kidney Margin (OD04348)	2.4
Colon cancer (OD06064)	0.0	Kidney malignant cancer (OD06204B)	0.0
Colon Margin (OD06064)	0.0	Kidney normal adjacent tissue (OD06204E)	0.0
Colon cancer (OD06159)	0.0	Kidney Cancer (OD04450-01)	3.4
Colon Margin (OD06159)	0.0	Kidney Margin (OD04450-03)	2.2
Colon cancer (OD06297-04)	0.0	Kidney Cancer 8120613	0.0
Colon Margin (OD06297-05)	0.0	Kidney Margin 8120614	0.0
CC Gr.2 ascend colon (ODO3921)	1.4	Kidney Cancer 9010320	0.0
CC Margin (ODO3921)	0.0	Kidney Margin 9010321	0.0
Colon cancer metastasis (OD06104)	0.0	Kidney Cancer 8120607	2.5
Lung Margin (OD06104)	0.0	Kidney Margin 8120608	1.2
Colon mets to lung (OD04451-01)	4.1	Normal Uterus	1.2
Lung Margin (OD04451-02)	0.0	Uterine Cancer 064011	2.7
Normal Prostate	3.3	Normal Thyroid	0.0
Prostate Cancer (OD04410)	0.0	Thyroid Cancer 064010	0.0
Prostate Margin (OD04410)	0.0	Thyroid Cancer A302152	0.0
Normal Ovary	8.0	Thyroid Margin A302153	0.0
Ovarian cancer (OD06283-03)	0.0	Normal Breast	2.4
Ovarian Margin (OD06283-07)	0.0	Breast Cancer (OD04566)	0.0
Ovarian Cancer 064008	4.2	Breast Cancer 1024	1.3
Ovarian cancer (OD06145)	0.0	Breast Cancer (OD04590-01)	7.1
Ovarian Margin (OD06145)	0.0	Breast Cancer Mets (OD04590-03)	4.4
Ovarian cancer (OD06455-03)	0.0	Breast Cancer Metastasis (OD04655-05)	100.0
Ovarian Margin (OD06455-07)	0.0	Breast Cancer 064006	1.2
Normal Lung	1.6	Breast Cancer 9100266	2.5
Invasive poor diff. lung adeno (ODO4945-01)	0.0	Breast Margin 9100265	0.0
Lung Margin (ODO4945-03)	0.0	Breast Cancer A209073	3.4
Lung Malignant Cancer	0.0	Breast Margin A2090734	0.0

(OD03126)			
Lung Margin (OD03126)	0.0	Breast cancer (OD06083)	3.2
Lung Cancer (OD05014A)	0.0	Breast cancer node metastasis (OD06083)	2.5
Lung Margin (OD05014B)	0.6	Normal Liver	0.0
Lung cancer (OD06081)	0.0	Liver Cancer 1026	0.0
Lung Margin (OD06081)	1.4	Liver Cancer 1025	2.1
Lung Cancer (OD04237-01)	0.0	Liver Cancer 6004-T	0.0
Lung Margin (OD04237-02)	0.4	Liver Tissue 6004-N	0.0
Ocular Melanoma Metastasis	0.0	Liver Cancer 6005-T	2.4
Ocular Melanoma Margin (Liver)	0.0	Liver Tissue 6005-N	0.0
Melanoma Metastasis	0.0	Liver Cancer 064003	0.0
Melanoma Margin (Lung)	0.0	Normal Bladder	0.0
Normal Kidney	0.0	Bladder Cancer 1023	0.0
Kidney Ca, Nuclear grade 2 (OD04338)	0.0	Bladder Cancer A302173	0.0
Kidney Margin (OD04338)	0.0	Normal Stomach	0.0
Kidney Ca Nuclear grade 1/2 (OD04339)	1.2	Gastric Cancer 9060397	0.8
Kidney Margin (OD04339)	0.0	Stomach Margin 9060396	0.9
Kidney Ca, Clear cell type (OD04340)	0.0	Gastric Cancer 9060395	0.0
Kidney Margin (OD04340)	0.0	Stomach Margin 9060394	1.4
Kidney Ca, Nuclear grade 3 (OD04348)	0.0	Gastric Cancer 064005	0.0

Table BME. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3247, Run 164390951	Tissue Name	Rel. Exp.(%) Ag3247, Run 164390951
Secondary Th1 act	1.6	HUVEC IL-1beta	0.6
Secondary Th2 act	0.6	HUVEC IFN gamma	4.1
Secondary Tr1 act	0.8	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	1.2
Secondary Th2 rest	0.8	HUVEC IL-11	3.1
Secondary Tr1 rest	0.0	Lung Microvascular EC none	17.1
Primary Th1 act	7.0	Lung Microvascular EC TNFalpha + IL-1beta	11.0
Primary Th2 act	3.5	Microvascular Dermal EC none	0.6
Primary Tr1 act	4.9	Microvascular Dermal EC TNFalpha + IL-1beta	0.7
Primary Th1 rest	0.6	Bronchial epithelium TNFalpha + IL1beta	100.0
Primary Th2 rest	1.2	Small airway epithelium none	1.8
Primary Tr1 rest	4.7	Small airway epithelium TNFalpha + IL-1beta	28.3
CD45RA CD4 lymphocyte act	0.7	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	2.7	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	3.0	Astrocytes rest	1.2
Secondary CD8 lymphocyte rest	4.2	Astrocytes TNFalpha + IL-1beta	0.6
Secondary CD8 lymphocyte act	0.7	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	1.3	KU-812 (Basophil) PMA/ionomycin	0.7

2ry Th1/Th2/Tr1_anti-CD95 CH11	0.7	CCD1106 (Keratinocytes) none	37.1
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	28.9
LAK cells IL-2	4.0	Liver cirrhosis	6.2
LAK cells IL-2+IL-12	2.1	Lupus kidney	1.1
LAK cells IL-2+IFN gamma	6.5	NCI-H292 none	2.5
LAK cells IL-2+ IL-18	4.7	NCI-H292 IL-4	1.3
LAK cells PMA/ionomycin	0.5	NCI-H292 IL-9	4.6
NK Cells IL-2 rest	1.3	NCI-H292 IL-13	1.1
Two Way MLR 3 day	1.8	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.5	HPAEC none	0.0
Two Way MLR 7 day	1.7	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	6.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.6	Lung fibroblast IL-4	0.0
Ramos (B cell) none	1.9	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	1.9	Lung fibroblast IL-13	0.0
B lymphocytes PWM	1.3	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	5.0	Dermal fibroblast CCD1070 rest	0.7
EOL-1 dbcAMP	3.0	Dermal fibroblast CCD1070 TNF alpha	0.7
EOL-1 dbcAMP PMA/ionomycin	0.6	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.7
Dendritic cells anti-CD40	0.0	IBD Colitis 2	0.0
Monocytes rest	0.6	IBD Crohn's	0.0
Monocytes LPS	0.0	Colon	2.7
Macrophages rest	0.0	Lung	0.6
Macrophages LPS	0.0	Thymus	1.0
HUVEC none	0.0	Kidney	7.0
HUVEC starved	5.0		

CNS_neurodegeneration_v1.0 Summary: Ag3247 This panel confirms the expression of this gene at low levels in the brains of an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.4 for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

General_screening_panel_v1.4 Summary: Ag3247 Highest expression of CG57462-01 is seen in samples derived from fetal brain (CT=26.5). In addition moderate expression of this gene is also observed in samples derived from whole brain, thalamus, Substantia nigra, cerebral cortex and hippocampus. Thus, expression of this gene could be used to differentiate between these samples and other samples on this panel. Also, this gene

may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, schizophrenia and depression.

The CG57462-01 gene encodes for a protein containing a patched domain (IPR003392). Patched, is a receptor for the morphogene sonic hedgehog. In *Drosophila melanogaster*, this protein associates with the smoothened protein to transduce hedgehog signals, leading to the activation of wingless, decapentaplegic and patched itself. It participates in cell interactions that establish pattern within the segment and imaginal disks during development. In mammals, the Hedgehog (HH) signaling pathway is involved in patterning and development of a variety of organ systems, including the nervous system, the skeletal system, the craniofacial structures, and the gastrointestinal tract. Abnormalities in this signaling cascade have been found in various developmental pathologies and neoplasms such as basal cell carcinoma, Niemann-Pick type II disease, holoprosencephaly. The abnormalities are associated with congenital or sporadic genetic alteration affecting function of different components of the HH signaling pathway, including SHH, PTCH, SMOH and GLI proteins (Ref. 2, 3). Thus, therapeutic modulation of the activity of the protein encoded by the CG57463-01 gene may be useful in the treatment of basal cell carcinoma, Niemann-Pick type II disease, and holoprosencephaly

References:

1. IPR003392: Patched family

The transmembrane protein, patched, is a receptor for the morphogene Sonic Hedgehog. In *Drosophila melanogaster*, this protein associates with the smoothened protein to transduce hedgehog signals, leading to the activation of wingless, decapentaplegic and patched itself. It participates in cell interactions that establish pattern within the segment and imaginal disks during development. The mouse homolog may play a role in epidermal development. The human Niemann-Pick C1 protein, defects in which cause Niemann-Pick type II disease, is also a member of this family. This protein is involved in the intracellular trafficking of cholesterol, and may play a role in vesicular trafficking in glia, a process that may be crucial for maintaining the structural functional integrity of nerve terminals.

2. Incardona JP, Roelink H. (2000) The role of cholesterol in Shh signaling and teratogen-induced holoprosencephaly. *Cell Mol Life Sci* 57(12):1709-19.

Holoprosencephaly, or an undivided forebrain, is a complex brain malformation associated with Sonic hedgehog (Shh) mutations. Other causes of holoprosencephaly have

converged upon the Shh signaling pathway: genetic and pharmacologic impairment of cholesterol synthesis, and the action of the steroidal alkaloid cyclopamine. This review focuses on recent studies aimed at determining how Shh signaling is affected by these causes of holoprosencephaly, whether they involve a common mechanism and the role played by cholesterol. Cholesterol is potentially important for both biogenesis of Shh and in signal transduction in Shh-responsive cells. Teratogens that induce holoprosencephaly appear to affect Shh signal transduction rather than Shh biogenesis. Analysis of these agents and other compounds that affect various aspects of cellular cholesterol distribution indicates that the role of cholesterol in Shh signal transduction is novel and complicated. The similarity of the Shh receptor, Patched (Ptc), to the Niemann-Pick C1 protein, which is involved in the vesicular trafficking of cholesterol, provides insight into the role of cholesterol and the action of compounds like cyclopamine.

PMID: 11130177

3. Oldak M, Grzela T, Lazarczyk M, Malejczyk J, Skopinski P. (2001) Clinical aspects of disrupted Hedgehog signaling (Review). *Int J Mol Med* 8(4):445-52.

The Hedgehog (HH) signaling pathway is involved in patterning and development of a variety of organ systems, including the nervous system, the skeletal system, the craniofacial structures, and the gastrointestinal tract. Recent evidence also implicates this signaling pathway in the postembryonic regulation of stem-cell number in epithelia and blood. The family of HH proteins consists of at least three different members, i.e., sonic HH (SHH), Indian HH (IHH), and desert HH (DHH). SHH is the most broadly expressed member of this family and is probably responsible for the major effects of this signaling pathway. The HH signal is received and transduced via a specific receptor complex composed of patched (PTCH) and smoothened (SMO) transmembrane proteins. Abnormalities in this signaling cascade have been found in various developmental pathologies and neoplasms such as basal cell carcinoma. The abnormalities are associated with congenital or sporadic genetic alteration affecting function of different components of the HH signaling pathway, including SHH, PTCH, SMO and GLI proteins.

PMID: 11562786

Panel 2.2 Summary: Ag3247 Expression of the CG57462-01 gene is highest in a metastatic breast cancer sample (CT = 29.8). Strikingly, this gene is expressed at higher levels in breast tumors when compared to their matched normal breast controls. Thus, expression of this gene may be used for the diagnosis of breast cancer. Furthermore, therapeutic modulation

of the activity of this gene or its protein product, using small molecule drugs, antibodies or protein therapeutics, may be of benefit in the treatment of breast cancer.

Panel 4D Summary: Ag3247 Expression of this gene is highest in bronchial epithelium treated with TNF alpha and IL-1 beta (CT = 30). In addition, expression of this gene is upregulated in activated small airway epithelium. Thus, therapeutic modulation of the activity of this gene may be of benefit in the treatment of asthma and emphysema.

NOV71

Expression of NOV71/CG57584-01 was assessed using the primer-probe set Ag3290, described in Table BNA. Results of the RTQ-PCR runs are shown in Tables BNB, and BNC.

Table BNA. Probe Name Ag3290

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ccctcagaggactggttactt-3'	22	1598	473
Probe	TET-5'-cacctctgcctgccacacctcag-3'-TAMRA	23	1629	474
Reverse	5'-ctacatgcagtggagcaagtct-3'	22	1658	475

Table BNB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3290, Run 210062016	Tissue Name	Rel. Exp.(%) Ag3290, Run 210062016
AD 1 Hippo	24.8	Control (Path) 3 Temporal Ctx	11.5
AD 2 Hippo	15.1	Control (Path) 4 Temporal Ctx	94.0
AD 3 Hippo	0.0	AD 1 Occipital Ctx	12.6
AD 4 Hippo	19.1	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	51.8	AD 3 Occipital Ctx	33.9
AD 6 Hippo	28.7	AD 4 Occipital Ctx	0.0
Control 2 Hippo	26.8	AD 5 Occipital Ctx	0.0
Control 4 Hippo	23.8	AD 6 Occipital Ctx	55.1
Control (Path) 3 Hippo	6.3	Control 1 Occipital Ctx	17.4
AD 1 Temporal Ctx	12.2	Control 2 Occipital Ctx	100.0
AD 2 Temporal Ctx	42.0	Control 3 Occipital Ctx	29.3
AD 3 Temporal Ctx	9.8	Control 4 Occipital Ctx	21.0
AD 4 Temporal Ctx	62.0	Control (Path) 1 Occipital Ctx	52.9
AD 5 Inf Temporal Ctx	14.0	Control (Path) 2 Occipital Ctx	15.4
AD 5 SupTemporal Ctx	26.6	Control (Path) 3 Occipital Ctx	9.8
AD 6 Inf Temporal Ctx	12.5	Control (Path) 4 Occipital Ctx	13.0
AD 6 Sup Temporal Ctx	2.3	Control 1 Parietal Ctx	13.8
Control 1 Temporal Ctx	39.0	Control 2 Parietal Ctx	76.3
Control 2 Temporal Ctx	39.8	Control 3 Parietal Ctx	21.3
Control 3 Temporal Ctx	0.0	Control (Path) 1 Parietal Ctx	50.3
Control 4 Temporal Ctx	12.4	Control (Path) 2 Parietal	16.0

		Ctx	
Control (Path) 1 Temporal Ctx	48.3	Control (Path) 3 Parietal Ctx	19.8
Control (Path) 2 Temporal Ctx	51.1	Control (Path) 4 Parietal Ctx	84.7

Table BNC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3290, Run 164331693	Tissue Name	Rel. Exp.(%) Ag3290, Run 164331693
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	14.9	HUVEC IL-11	0.0
Secondary Tr1 rest	3.6	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	4.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	9.4	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	36.6	Small airway epithelium none	9.1
Primary Tr1 rest	16.2	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	100.0
CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	38.2
CD8 lymphocyte act	0.0	Astrocytes rest	4.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	3.7
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.5
2ry Th1/Th2/Tr1_anti-CD95 CH11	6.8	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	2.9	Liver cirrhosis	0.0
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	4.6	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.5
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	4.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	12.8	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	4.4	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and	0.0	Dermal fibroblast CCD1070 rest	17.6

Crohns-M			
112378 Crohns-M	1.0	113494 Syn Fluid Cells RA	12.8
112390 Match Control Crohns-M	7.9	113499 Cartilage4 RA	12.8
112726 Crohns-M	5.0	113500 Bone4 RA	19.5
112731 Match Control Crohns-M	5.9	113501 Synovium4 RA	14.0
112380 Ulcer Col-F	5.2	113502 Syn Fluid Cells4 RA	6.4
112734 Match Control Ulcer Col-F	100.0	113495 Cartilage3 RA	11.5
112384 Ulcer Col-F	11.0	113496 Bone3 RA	13.8
112737 Match Control Ulcer Col-F	1.7	113497 Synovium3 RA	5.6
112386 Ulcer Col-F	4.5	113498 Syn Fluid Cells3 RA	15.3
112738 Match Control Ulcer Col-F	5.3	117106 Normal Cartilage Rep20	5.9
112381 Ulcer Col-M	3.1	113663 Bone3 Normal	0.4
112735 Match Control Ulcer Col-M	2.3	113664 Synovium3 Normal	0.0
112382 Ulcer Col-M	6.7	113665 Syn Fluid Cells3 Normal	0.0
112394 Match Control Ulcer Col-M	2.4	117107 Normal Cartilage Rep22	3.0
112383 Ulcer Col-M	6.6	113667 Bone4 Normal	2.8
112736 Match Control Ulcer Col-M	3.0	113668 Synovium4 Normal	3.4
112423 Psoriasis-F	4.2	113669 Syn Fluid Cells4 Normal	4.3

Table BOE. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag1810, Run 207742479	Rel. Exp.(%) Ag1811, Run 207776005	Rel. Exp.(%) Ag3011, Run 211010257	Tissue Name	Rel. Exp.(%) Ag1810, Run 207742479	Rel. Exp.(%) Ag1811, Run 207776005	Rel. Exp.(%) Ag3011, Run 211010257
AD 1 Hippo	7.8	11.3	9.1	Control (Path) 3 Temporal Ctx	4.3	6.9	4.0
AD 2 Hippo	13.1	21.9	15.2	Control (Path) 4 Temporal Ctx	20.7	26.6	23.5
AD 3 Hippo	4.6	6.7	5.3	AD 1 Occipital Ctx	12.7	21.3	13.3
AD 4 Hippo	4.6	6.2	3.7	AD 2 Occipital Ctx (Missing)	0.2	0.0	0.0
AD 5 Hippo	100.0	100.0	100.0	AD 3 Occipital Ctx	6.1	10.9	6.9
AD 6 Hippo	19.9	19.9	18.8	AD 4 Occipital Ctx	12.1	16.7	13.4
Control 2 Hippo	11.9	19.1	12.3	AD 5 Occipital Ctx	29.1	41.2	21.5
Control 4 Hippo	3.9	7.0	3.4	AD 6 Occipital Ctx	17.3	17.4	31.6

Control (Path) 3 Hippo	3.7	5.0	3.6	Control 1 Occipital Ctx	3.7	5.7	3.4
AD 1 Temporal Ctx	11.7	15.0	9.5	Control 2 Occipital Ctx	59.9	81.2	62.0
AD 2 Temporal Ctx	20.9	22.7	17.7	Control 3 Occipital Ctx	13.9	21.0	13.5
AD 3 Temporal Ctx	5.8	9.0	5.4	Control 4 Occipital Ctx	3.7	8.8	3.8
AD 4 Temporal Ctx	15.2	17.8	14.1	Control (Path) 1 Occipital Ctx	51.4	58.6	54.7
AD 5 Inf Temporal Ctx	91.4	95.3	82.4	Control (Path) 2 Occipital Ctx	8.9	13.9	11.3
AD 5 Sup Temporal Ctx	25.3	35.4	33.0	Control (Path) 3 Occipital Ctx	2.8	4.5	3.3
AD 6 Inf Temporal Ctx	27.4	27.7	30.4	Control (Path) 4 Occipital Ctx	17.2	15.9	13.9
AD 6 Sup Temporal Ctx	28.7	26.8	32.1	Control 1 Parietal Ctx	5.5	7.4	4.9
Control 1 Temporal Ctx	3.4	5.9	2.8	Control 2 Parietal Ctx	31.9	38.7	35.6
Control 2 Temporal Ctx	34.4	42.9	28.9	Control 3 Parietal Ctx	14.9	20.9	15.1
Control 3 Temporal Ctx	6.4	12.8	7.7	Control (Path) 1 Parietal Ctx	47.3	53.2	51.8
Control 3 Temporal Ctx	6.0	11.3	8.2	Control (Path) 2 Parietal Ctx	14.5	15.9	16.2
Control (Path) 1 Temporal Ctx	37.6	37.9	39.8	Control (Path) 3 Parietal Ctx	3.6	5.6	4.3
Control (Path) 2 Temporal Ctx	24.1	30.1	26.8	Control (Path) 4 Parietal Ctx	25.2	35.4	31.6

Table BOF, Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag1810, Run 146338117	Rel. Exp.(%) Ag1811, Run 147104851	Rel. Exp.(%) Ag1811, Run 165544641	Rel. Exp.(%) Ag3011, Run 167927169
Liver adenocarcinoma	3.8	3.3	2.3	7.0
Pancreas	0.3	0.0	0.6	0.4
Pancreatic ca. CAPAN 2	0.0	0.0	0.2	0.1
Adrenal gland	1.1	2.2	1.7	1.2
Thyroid	0.6	1.8	1.1	0.4
Salivary gland	0.9	1.7	0.8	1.4
Pituitary gland	1.2	1.5	0.6	0.7

Brain (fetal)	2.8	4.1	8.8	15.1
Brain (whole)	48.0	49.0	100.0	93.3
Brain (amygdala)	32.1	47.6	84.1	48.0
Brain (cerebellum)	9.9	13.9	44.4	60.7
Brain (hippocampus)	75.8	86.5	88.3	31.6
Brain (substantia nigra)	10.8	23.0	49.7	39.8
Brain (thalamus)	18.0	29.9	71.7	28.5
Cerebral Cortex	100.0	100.0	77.4	100.0
Spinal cord	11.3	17.8	28.5	17.8
glio/astro U87-MG	0.0	0.0	0.0	0.0
glio/astro U-118-MG	0.0	0.0	0.0	0.0
astrocytoma SW1783	0.0	0.0	0.0	0.1
neuro*; met SK-N-AS	23.7	30.4	15.4	13.3
astrocytoma SF-539	0.0	0.0	0.2	0.0
astrocytoma SNB-75	0.0	0.1	0.1	0.2
glioma SNB-19	0.0	0.0	0.0	0.0
glioma U251	0.0	0.0	0.1	0.0
glioma SF-295	0.1	0.0	0.0	0.0
Heart (fetal)	3.9	2.5	0.9	3.0
Heart	0.6	0.6	1.5	1.4
Skeletal muscle (fetal)	11.5	18.3	2.4	6.5
Skeletal muscle	0.2	0.1	1.0	0.4
Bone marrow	0.9	1.8	3.0	0.5
Thymus	5.4	7.2	4.7	9.5
Spleen	14.3	25.9	17.4	11.9
Lymph node	7.9	15.9	29.7	11.5
Colorectal	1.5	3.0	1.1	1.6
Stomach	3.8	4.9	2.8	1.9
Small intestine	2.6	4.6	5.3	1.6
Colon ca. SW480	0.0	0.0	0.0	0.0
Colon ca.* SW620(SW480 met)	0.0	0.0	0.0	0.0
Colon ca. HT29	0.0	0.0	0.0	0.0
Colon ca. HCT-116	0.0	0.0	0.0	0.0
Colon ca. CaCo-2	0.0	0.1	0.0	0.0
Colon ca. tissue(ODO3866)	0.7	2.0	1.1	0.7
Colon ca. HCC-2998	0.0	0.0	0.2	0.0
Gastric ca.* (liver met) NCI-N87	0.2	0.1	0.0	0.3
Bladder	0.1	0.1	0.1	0.4
Trachea	1.8	3.8	3.8	0.8
Kidney	6.3	11.8	22.2	38.2
Kidney (fetal)	2.0	4.5	2.8	13.5
Renal ca. 786-0	0.0	0.0	0.0	0.0
Renal ca. A498	0.0	0.0	0.0	0.1
Renal ca. RXF 393	0.0	0.0	0.0	0.0
Renal ca. ACHN	0.0	0.0	0.0	0.0
Renal ca. UO-31	0.0	0.0	0.0	0.0
Renal ca. TK-10	0.0	0.0	0.0	0.0
Liver	0.4	1.4	1.2	2.0
Liver (fetal)	0.4	1.3	1.0	0.6
Liver ca. (hepatoblast) HepG2	0.0	0.0	0.0	0.0

Lung	6.7	11.9	9.3	8.0
Lung (fetal)	5.1	7.1	4.7	3.3
Lung ca. (small cell) LX-1	0.0	0.0	0.0	0.0
Lung ca. (small cell) NCI-H69	4.2	3.2	1.6	3.5
Lung ca. (s.cell var.) SHP-77	0.0	0.1	0.0	0.0
Lung ca. (large cell)NCI-H460	0.0	0.0	0.0	0.0
Lung ca. (non-sm. cell) A549	0.0	0.1	0.0	0.4
Lung ca. (non-s.cell) NCI-H23	0.5	0.3	0.4	0.7
Lung ca. (non-s.cell) HOP-62	0.0	0.0	0.0	0.1
Lung ca. (non-s.cl) NCI- H522	6.9	5.6	1.7	11.8
Lung ca. (squam.) SW 900	0.0	0.0	0.0	0.0
Lung ca. (squam.) NCI- H596	0.6	1.6	0.7	2.2
Mammary gland	3.0	4.0	1.8	2.3
Breast ca.* (pl.ef) MCF- 7	0.0	0.0	0.0	0.0
Breast ca.* (pl.ef) MDA-MB-231	0.0	0.0	0.0	0.0
Breast ca.* (pl.ef) T47D	0.0	0.0	0.0	0.0
Breast ca. BT-549	0.0	0.0	0.0	0.0
Breast ca. MDA-N	0.0	0.0	0.0	0.0
Ovary	2.2	1.0	0.4	0.4
Ovarian ca. OVCAR-3	1.2	1.1	0.8	1.5
Ovarian ca. OVCAR-4	0.1	0.1	0.0	0.2
Ovarian ca. OVCAR-5	0.0	0.1	0.0	0.0
Ovarian ca. OVCAR-8	1.4	2.3	0.9	1.1
Ovarian ca. IGROV-1	0.0	0.0	0.1	0.1
Ovarian ca.* (ascites) SK-OV-3	0.0	0.0	0.0	0.1
Uterus	1.8	2.7	4.0	1.4
Placenta	3.2	4.5	2.8	0.6
Prostate	0.3	0.6	0.8	0.4
Prostate ca.* (bone met)PC-3	0.0	0.0	0.0	0.0
Testis	0.4	0.3	0.4	0.1
Melanoma Hs688(A).T	0.0	0.0	0.0	0.0
Melanoma* (met) Hs688(B).T	0.0	0.0	0.0	0.0
Melanoma UACC-62	0.0	0.0	0.0	0.0
Melanoma M14	0.0	0.0	0.0	0.0
Melanoma LOX IMVI	0.0	0.0	0.0	0.0
Melanoma* (met) SK- MEL-5	0.4	0.1	0.1	0.9
Adipose	2.4	4.0	3.0	8.0

Table BOG. Panel 2D

Tissue Name	Rel. Exp.(%)	Rel. Exp.(%)	Tissue Name	Rel. Exp.(%)	Rel. Exp.(%)
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(OD04237-02)			T		
Ocular Mel Met to Liver (ODO4310)	0.6	0.9	Liver Tissue 6005-N	2.9	1.5
Liver Margin (ODO4310)	2.4	2.1	Normal Bladder	3.1	2.6
Melanoma Mets to Lung (OD04321)	4.5	3.8	Bladder Cancer 1023	3.3	1.4
Lung Margin (OD04321)	15.2	18.7	Bladder Cancer A302173	2.7	2.6
Normal Kidney	54.0	45.1	Bladder Cancer (OD04718-01)	4.8	3.1
Kidney Ca, Nuclear grade 2 (OD04338)	2.2	1.6	Bladder Normal Adjacent (OD04718-03)	5.7	3.8
Kidney Margin (OD04338)	23.3	14.4	Normal Ovary	1.2	1.7
Kidney Ca Nuclear grade 1/2 (OD04339)	2.7	1.0	Ovarian Cancer 064008	7.2	5.0
Kidney Margin (OD04339)	94.0	84.1	Ovarian Cancer (OD04768-07)	1.5	0.7
Kidney Ca, Clear cell type (OD04340)	27.0	22.8	Ovary Margin (OD04768-08)	3.4	3.8
Kidney Margin (OD04340)	54.7	52.5	Normal Stomach	8.0	7.1
Kidney Ca, Nuclear grade 3 (OD04348)	2.7	1.7	Gastric Cancer 9060358	5.1	3.6
Kidney Margin (OD04348)	15.0	9.2	Stomach Margin 9060359	8.7	7.9
Kidney Cancer (OD04622-01)	11.5	5.6	Gastric Cancer 9060395	7.1	6.6
Kidney Margin (OD04622-03)	17.6	9.0	Stomach Margin 9060394	14.5	13.3
Kidney Cancer (OD04450-01)	0.4	0.5	Gastric Cancer 9060397	3.3	2.9
Kidney Margin (OD04450-03)	18.7	12.1	Stomach Margin 9060396	7.2	5.0
Kidney Cancer 8120607	1.7	1.0	Gastric Cancer 064005	21.8	10.4

Table BOH. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1810, Run 162733751	Rel. Exp.(%) Ag1811, Run 147164258	Rel. Exp.(%) Ag3011, Run 164043491	Tissue Name	Rel. Exp.(%) Ag1810, Run 162733751	Rel. Exp.(%) Ag1811, Run 147164258	Rel. Exp.(%) Ag3011, Run 164043491
Secondary Th1 act	42.3	40.9	30.1	HUVEC IL-1beta	3.8	4.5	4.5
Secondary Th2 act	37.1	43.8	32.5	HUVEC IFN gamma	18.8	15.7	13.6
Secondary Tr1 act	47.6	54.0	35.8	HUVEC TNF alpha + IFN gamma	1.4	1.1	0.6
Secondary Th1 rest	8.0	11.5	7.2	HUVEC TNF alpha + IL4	2.5	1.8	1.2
Secondary Th2 rest	13.4	11.6	11.9	HUVEC IL-11	12.2	12.0	7.5
Secondary Tr1 rest	12.8	12.8	9.3	Lung Microvascular EC none	13.1	11.3	10.2
Primary Th1 act	21.3	18.9	14.9	Lung Microvascular EC TNFalpha + IL-	3.8	4.4	2.5

				1beta			
Primary Th2 act	29.5	39.8	26.1	Microvascular Dermal EC none	37.1	27.4	29.3
Primary Tr1 act	33.9	42.3	27.7	Microvascular Dermal EC TNFalpha + IL- 1beta	10.7	9.5	7.4
Primary Th1 rest	44.8	36.1	34.6	Bronchial epithelium TNFalpha + IL1beta	0.0	0.0	0.0
Primary Th2 rest	25.9	20.6	28.9	Small airway epithelium none	0.0	0.0	0.0
Primary Tr1 rest	22.2	11.0	15.1	Small airway epithelium TNFalpha + IL- 1beta	0.0	0.0	0.0
CD45RA CD4 lymphocyte act	11.6	11.3	8.7	Coronary artery SMC rest	0.3	0.3	0.3
CD45RO CD4 lymphocyte act	41.8	35.1	29.3	Coronary artery SMC TNFalpha + IL-1beta	0.2	0.1	0.1
CD8 lymphocyte act	31.4	24.1	23.3	Astrocytes rest	0.0	0.0	0.0
Secondary CD8 lymphocyte rest	42.6	25.3	31.6	Astrocytes TNFalpha + IL- 1beta	0.0	0.0	0.0
Secondary CD8 lymphocyte act	28.7	17.1	20.4	KU-812 (Basophil) rest	0.1	0.3	0.2
CD4 lymphocyte none	6.2	3.6	4.6	KU-812 (Basophil) PMA/ionomycin	5.6	2.9	2.9
2ry Th1/Th2/Tr1_anti- CD95 CH11	20.4	16.0	18.9	CCD1106 (Keratinocytes) none	0.0	0.1	0.0
LAK cells rest	12.9	9.6	7.9	CCD1106 (Keratinocytes) TNFalpha + IL- 1beta	0.0	0.0	0.0
LAK cells IL-2	38.7	28.3	30.1	Liver cirrhosis	0.6	0.5	0.8
LAK cells IL-2+IL- 12	27.4	18.4	20.2	Lupus kidney	0.3	0.5	0.4
LAK cells IL- 2+IFN gamma	42.9	29.3	26.6	NCI-H292 none	0.0	0.0	0.0
LAK cells IL-2+ IL-18	45.7	22.7	20.3	NCI-H292 IL-4	0.0	0.0	0.0
LAK cells PMA/ionomycin	31.6	26.6	20.6	NCI-H292 IL-9	0.0	0.0	0.0
NK Cells IL-2 rest	21.9	17.9	15.5	NCI-H292 IL-13	0.1	0.0	0.0
Two Way MLR 3 day	20.3	19.9	14.4	NCI-H292 IFN gamma	0.0	0.0	0.0
Two Way MLR 5 day	23.2	16.2	15.1	HPAEC none	13.0	14.5	9.4
Two Way MLR 7 day	16.7	16.3	17.9	HPAEC TNF alpha + IL-1 beta	4.6	5.6	4.4
PBMC rest	5.9	4.1	4.5	Lung fibroblast none	0.0	0.0	0.0
PBMC PWM	79.6	54.7	84.1	Lung fibroblast TNF alpha + IL-1 beta	0.0	0.0	0.0
PBMC PHA-L	39.8	31.6	39.0	Lung fibroblast IL-	0.0	0.0	0.0

				4			
Ramos (B cell) none	10.2	7.5	8.7	Lung fibroblast IL-9	0.0	0.0	0.0
Ramos (B cell) ionomycin	20.9	12.2	13.6	Lung fibroblast IL-13	0.0	0.0	0.0
B lymphocytes PWM	96.6	100.0	100.0	Lung fibroblast IFN gamma	0.1	0.0	0.0
B lymphocytes CD40L and IL-4	100.0	59.9	53.2	Dermal fibroblast CCD1070 rest	0.0	0.0	0.0
EOL-1 dbcAMP	6.2	5.4	3.9	Dermal fibroblast CCD1070 TNF alpha	27.0	22.1	22.5
EOL-1 dbcAMP PMA/ionomycin	61.1	46.3	38.4	Dermal fibroblast CCD1070 IL-1 beta	0.0	0.1	0.0
Dendritic cells none	3.1	2.2	1.7	Dermal fibroblast IFN gamma	0.0	0.0	0.0
Dendritic cells LPS	5.3	3.8	4.0	Dermal fibroblast IL-4	0.0	0.0	0.0
Dendritic cells anti-CD40	1.1	0.9	1.3	IBD Colitis 2	0.7	0.9	0.6
Monocytes rest	1.3	0.7	0.9	IBD Crohn's	0.4	0.2	0.2
Monocytes LPS	1.4	1.0	1.1	Colon	8.3	6.8	5.7
Macrophages rest	1.8	1.4	1.7	Lung	8.5	7.5	5.8
Macrophages LPS	0.7	0.7	0.4	Thymus	21.2	27.2	21.3
HUVEC none	11.4	7.2	7.5	Kidney	9.3	8.3	7.6
HUVEC starved	17.7	13.7	10.0				

Table BOI. Panel CNS_1

Tissue Name	Rel. Exp.(%) Ag1811, Run 171628390	Tissue Name	Rel. Exp.(%) Ag1811, Run 171628390
BA4 Control	27.7	BA17 PSP	31.9
BA4 Control2	52.1	BA17 PSP2	10.1
BA4 Alzheimer's2	6.0	Sub Nigra Control	36.1
BA4 Parkinson's	51.4	Sub Nigra Control2	20.3
BA4 Parkinson's2	93.3	Sub Nigra Alzheimer's2	5.9
BA4 Huntington's	13.2	Sub Nigra Parkinson's2	32.5
BA4 Huntington's2	7.7	Sub Nigra Huntington's	35.1
BA4 PSP	7.7	Sub Nigra Huntington's2	18.6
BA4 PSP2	17.3	Sub Nigra PSP2	5.5
BA4 Depression	19.2	Sub Nigra Depression	8.8
BA4 Depression2	11.1	Sub Nigra Depression2	3.0
BA7 Control	42.6	Glob Palladus Control	17.4
BA7 Control2	35.6	Glob Palladus Control2	19.3
BA7 Alzheimer's2	5.9	Glob Palladus Alzheimer's	4.0
BA7 Parkinson's	21.2	Glob Palladus Alzheimer's2	8.5
BA7 Parkinson's2	61.6	Glob Palladus Parkinson's	100.0
BA7 Huntington's	61.1	Glob Palladus Parkinson's2	15.3
BA7 Huntington's2	75.3	Glob Palladus PSP	3.9
BA7 PSP	29.3	Glob Palladus PSP2	8.4
BA7 PSP2	17.6	Glob Palladus Depression	4.1
BA7 Depression	13.6	Temp Pole Control	14.0
BA9 Control	21.2	Temp Pole Control2	70.7
BA9 Control2	90.1	Temp Pole Alzheimer's	3.8

BA9 Alzheimer's	4.0	Temp Pole Alzheimer's2	5.4
BA9 Alzheimer's2	12.6	Temp Pole Parkinson's	32.8
BA9 Parkinson's	40.9	Temp Pole Parkinson's2	28.1
BA9 Parkinson's2	61.1	Temp Pole Huntington's	38.4
BA9 Huntington's	67.4	Temp Pole PSP	3.8
BA9 Huntington's2	17.8	Temp Pole PSP2	2.7
BA9 PSP	13.8	Temp Pole Depression2	8.9
BA9 PSP2	5.1	Cing Gyr Control	60.7
BA9 Depression	14.0	Cing Gyr Control2	29.7
BA9 Depression2	14.5	Cing Gyr Alzheimer's	16.7
BA17 Control	61.6	Cing Gyr Alzheimer's2	5.9
BA17 Control2	56.3	Cing Gyr Parkinson's	43.5
BA17 Alzheimer's2	9.0	Cing Gyr Parkinson's2	45.7
BA17 Parkinson's	49.3	Cing Gyr Huntington's	78.5
BA17 Parkinson's2	74.7	Cing Gyr Huntington's2	28.5
BA17 Huntington's	44.4	Cing Gyr PSP	13.1
BA17 Huntington's2	42.9	Cing Gyr PSP2	6.1
BA17 Depression	14.5	Cing Gyr Depression	7.7
BA17 Depression2	37.9	Cing Gyr Depression2	14.1

AI_comprehensive_panel_v1.0 Summary: Ag3011 CG56761-01 gene expression is upregulated in arthritis tissue as compared to normal joint tissue. It is also expressed in matched control gut tissue and at low levels in pulmonary tissue. The consistent induction of this transcript in arthritic tissue suggests that the protein encoded for by this transcript may be involved in the pathological processes associated with arthritis and may serve as a relevant target for therapeutic intervention.

CNS_neurodegeneration_v1.0 Summary: Ag1810/Ag1811/Ag3011 Results from three experiments using different probe/primer sets are in excellent agreement. This panel confirms the expression of the CG56761-01 gene at low levels in the brains of an independent group of individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. Please see Panel 1.3D for a discussion of the potential utility of this gene in treatment of central nervous system disorders.

Panel 1.3D Summary: Ag1810/Ag1811/Ag3011 Three experiments with three different probe and primer sets produce results that are in excellent agreement. The CG56761-01 gene is expressed at moderate to high levels in all regions of the central nervous system examined, including amygdala, hippocampus, substantia nigra, thalamus, cerebellum, cerebral cortex, and spinal cord. Thus, expression of this gene may be used to distinguish brain from the other samples on this panel. In addition, this gene may play a role in central nervous system disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis,

Interestingly, expression of this gene appears to be highly down-regulated in CNS cancer cell lines. Thus, modulation of the activity of this gene product may be of benefit in the treatment of cancers of the central nervous system.

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NOV73

Expression of NOV73/CG57313-01 was assessed using the primer-probe set Ag3185, described in Table BAA.

Table BAA. Probe Name Ag3185

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ccatcttctgtgtggacagttac-3'	22	779	485
Probe	TET-5'-catgtatatataccagcgaacagttcca-3'-TAMRA	28	804	486
Reverse	5'-agaagtttgccctcattctgat-3'	22	833	487

Panel 1.3D Summary: Ag3185 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

5

NOV74

Expression of NOV74/CG57315-01 was assessed using the primer-probe set Ag3186, described in Table BBA. Results of the RTQ-PCR runs are shown in Tables BBB, and BBC.

10

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gagttgcattgtgtgtgttg-3'	22	610	488
Probe	TET-5'-tcatttccttgcataccttctctca-3'-TAMRA	27	638	489
Reverse	5'-caatgaagccatgatgacacaag-3'	22	667	490

Table BBB. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag3186, Run 209859516	Tissue Name	Rel. Exp.(%) Ag3186, Run 209859516
AD 1 Hippo	32.5	Control (Path) 3 Temporal Ctx	0.0
AD 2 Hippo	100.0	Control (Path) 4 Temporal Ctx	0.0
AD 3 Hippo	29.9	AD 1 Occipital Ctx	0.0
AD 4 Hippo	38.7	AD 2 Occipital Ctx (Missing)	0.0
AD 5 hippo	0.0	AD 3 Occipital Ctx	0.0
AD 6 Hippo	76.8	AD 4 Occipital Ctx	5.4
Control 2 Hippo	55.5	AD 5 Occipital Ctx	0.0
Control 4 Hippo	92.7	AD 6 Occipital Ctx	0.0
Control (Path) 3 Hippo	32.8	Control 1 Occipital Ctx	0.0
AD 1 Temporal Ctx	0.0	Control 2 Occipital Ctx	0.0
AD 2 Temporal Ctx	13.2	Control 3 Occipital Ctx	7.6
AD 3 Temporal Ctx	0.0	Control 4 Occipital Ctx	0.0
AD 4 Temporal Ctx	0.0	Control (Path) 1 Occipital Ctx	42.0
AD 5 Inf Temporal Ctx	0.0	Control (Path) 2 Occipital Ctx	0.0
AD 5 SupTemporal Ctx	87.1	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	0.0	Control (Path) 4 Occipital Ctx	0.0
AD 6 Sup Temporal Ctx	0.0	Control 1 Parietal Ctx	0.0
Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	0.0
Control 2 Temporal Ctx	0.0	Control 3 Parietal Ctx	0.0
Control 3 Temporal Ctx	11.2	Control (Path) 1 Parietal Ctx	7.0

Control 4 Temporal Ctx	0.0	Control (Path) 2 Parietal Ctx	0.0
Control (Path) 1 Temporal Ctx	16.2	Control (Path) 3 Parietal Ctx	0.0
Control (Path) 2 Temporal Ctx	0.0	Control (Path) 4 Parietal Ctx	0.0

Table BBC. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag3186, Run 167994623	Tissue Name	Rel. Exp.(%) Ag3186, Run 167994623
Liver adenocarcinoma	20.4	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	0.0	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	0.0	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	11.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	3.6	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	15.4	Lung (fetal)	0.0
Brain (substantia nigra)	0.0	Lung ca. (small cell) LX-1	0.0
Brain (thalamus)	14.7	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	0.0
Spinal cord	38.2	Lung ca. (large cell) NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	9.7
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	36.3
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	9.7
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-H522	0.0
astrocytoma SF-539	15.6	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	0.0	Mammary gland	0.0
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	21.6
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	0.0	Breast ca. BT-549	9.0
Skeletal muscle (fetal)	0.0	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	0.0
Thymus	0.0	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	8.0
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	24.7	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	100.0
Small intestine	0.0	Uterus	0.0

Colon ca. SW480	16.2	Placenta	0.0
Colon ca. * SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca. * (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	32.1
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	0.0	Melanoma UACC-62	0.0
Gastric ca. * (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	21.6	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

CNS_neurodegeneration_v1.0 Summary: Ag3186 This panel demonstrates the expression of the CG57315-01 gene at low levels in the brains of a group of several individuals. However, no differential expression of this gene was detected between Alzheimer's diseased postmortem brains and those of non-demented controls in this experiment. The CG57315-01 gene encodes a putative GPCR. Several neurotransmitter receptors are GPCRs, including the dopamine receptor family, the serotonin receptor family, the GABAB receptor, muscarinic acetylcholine receptors, and others; thus this GPCR may represent a novel neurotransmitter receptor. Targeting various neurotransmitter receptors (dopamine, serotonin) has proven to be an effective therapy in psychiatric illnesses such as schizophrenia, bipolar disorder, and depression. Furthermore, the cerebral cortex and hippocampus are regions of the brain that are known to be involved in Alzheimer's disease, seizure disorders, and in the normal process of memory formation. Therefore, therapeutic modulation of this gene or its protein product may be beneficial in the treatment of one or more of these diseases, as may stimulation and/or blockade of the receptor coded for by the gene.

Panel 1.3D Summary: Ag3186 Low levels of expression of the CG57315-01 gene are seen exclusively in an ovarian cancer sample (CT = 34.7). Therefore, expression of this gene may be used to distinguish ovarian cancer cell lines from the other samples on this panel. Furthermore, therapeutic modulation of the activity of the GPCR encoded by this gene may be beneficial in the treatment of ovarian cancer.

Panel 4D Summary: Ag3186 Expression of CG57315-01 is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV75

Panel 2.2 Summary: Ag3233 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV78

5 Expression of NOV78/CG57425-01 was assessed using the primer-probe sets Ag1703 and Ag1747, described in Tables BEA and BEB. Results of the RTQ-PCR runs are shown in Table BEC.

Table BEA. Probe Name Ag1703

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gaggtgcttcaacaaaggaat-3'	22	108	497
Probe	TET-5'-tcggttactcccttactgaatcccttca-3'-TAMRA	28	64	498
Reverse	5'-gcttggttcacttgctgatttc-3'	22	30	499

Table BEB. Probe Name Ag1747

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gaggtgcttcaacaaaggaat-3'	22	108	500
Probe	TET-5'-tcggttactcccttactgaatcccttca-3'-TAMRA	28	64	501
Reverse	5'-gcttggttcacttgctgatttc-3'	22	30	502

Table BEC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag1747, Run 165808155	Tissue Name	Rel. Exp.(%) Ag1747, Run 165808155
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	5.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	2.6	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	10.3	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	0.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	3.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	10.2	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	7.2	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95	2.9	CCD1106 (Keratinocytes) none	0.0

CH11			
LAK cells rest	4.1	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	100.0
LAK cells IL-2+IL-12	7.5	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	13.1	NCI-H292 none	0.0
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	15.3	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	5.9	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	10.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	6.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	0.0
B lymphocytes CD40L and IL-4	8.2	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	4.2	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	0.0	Dermal fibroblast IL-4	0.0
Dendritic cells anti-CD40	0.0	IBD Colitis 2	12.4
Monocytes rest	0.0	IBD Crohn's	7.9
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	0.0	Lung	0.0
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	0.0	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: Ag1703 Expression of the CG57425-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel due to a probable probe or chemistry failure (data not shown). Ag1747 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

5 **Panel 2.2 Summary:** Ag1703 Expression of the CG57425-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel due to a probable probe or chemistry failure (data not shown). Ag1747 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

10 **Panel 4D Summary:** Ag1703 Expression of CG57425-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel due to a probable probe or chemistry failure (data not shown). Ag1747 Low levels of expression of this gene are detected in a liver cirrhosis sample (CT = 33.1). Furthermore, expression of this gene is not detected in normal

liver in Panel 1.3D, suggesting that its expression is unique to liver cirrhosis. This gene encodes a putative GPCR; therefore, antibodies or small molecule therapeutics could reduce or inhibit fibrosis that occurs in liver cirrhosis. In addition, antibodies to this putative GPCR could also be used for the diagnosis of liver cirrhosis.

5 NOV80

Expression of gene CG56766-01 was assessed using the primer-probe set Ag3013, described in Table BPA.

Table BPA. Probe Name Ag3013

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-tacactgtgtgcacgccaataa-3'	22	888	503
Probe	TET-5'-cccttgattactgctgaggaaca-3'-TAMRA	26	914	504
Reverse	5'-ttttcaaggcgtccttaaatc-3'	22	942	505

CNS_neurodegeneration_v1.0 Summary: Ag3013 Expression of the CG56766-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 1.3D Summary: Ag3013 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown). The CG56766-01 gene encodes a G protein-coupled receptor (GPCR), a type of cell surface receptor involved in signal transduction. This gene product is most similar to members of the odorant receptor subfamily of GPCRs. Based on analogy to other odorant receptor genes, we predict that expression of this gene may be highest in nasal epithelium, a sample not represented on this panel.

Panel 4D Summary: Ag3013 Expression of the CG56766-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV81

Expression of NOV81A/CG57847-01 and NOV81B/CG57847-02 was assessed using the primer-probe set Ag3347, described in Table BQA. Results of the RTQ-PCR runs are shown in Table BQB. Please note that CG57847-02 represents a full-length physical clone of the CG57847-01 gene, validating the prediction of the gene sequence.

Table BQA. Probe Name Ag3347

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-attgatttggttgctacttg-3'	22	866	506

Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	0.0	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	75.3	CNS cancer (glio) SNB-19	0.0
Lung ca. SHP-77	100.0	CNS cancer (glio) SF-295	0.0
Lung ca. A549	0.0	Brain (Amygdala) Pool	1.9
Lung ca. NCI-H526	0.0	Brain (cerebellum)	0.0
Lung ca. NCI-H23	21.9	Brain (fetal)	0.0
Lung ca. NCI-H460	8.2	Brain (Hippocampus) Pool	0.0
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	0.0
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	0.0
Liver	0.0	Brain (Thalamus) Pool	0.0
Fetal Liver	1.5	Brain (whole)	0.0
Liver ca. HepG2	0.0	Spinal Cord Pool	0.0
Kidney Pool	0.0	Adrenal Gland	0.0
Fetal Kidney	6.1	Pituitary gland Pool	0.0
Renal ca. 786-0	0.0	Salivary Gland	4.7
Renal ca. A498	0.0	Thyroid (female)	0.0
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.0	Pancreas Pool	5.3

CNS_neurodegeneration_v1.0 Summary: Ag3347 Results from one experiment with the CG57847-01 gene are not included. The amp plot indicates that there were experimental difficulties with this run.

General_screening_panel_v1.4 Summary: Ag3347 Expression of the CG57847-01 gene is restricted to two lung cancer cell lines. Therefore, expression of this gene may be used to distinguish lung cancer cell lines from the other samples on this panel. In addition, therapeutic modulation of the activity of this gene or its protein product, through the use of small molecule drugs, protein therapeutics or antibodies, might be beneficial in the treatment of lung cancer.

Panel 4D Summary: Ag3347 Expression of the CG57847-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV82

Expression of NOV82/CG57845-01 was assessed using the primer-probe set Ag3346, described in Table BRA. Results of the RTQ-PCR runs are shown in Table BRB.

Table BRA. Probe Name Ag3346

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-actcttcacagtgtgctgatg-3'	22	317	509
Probe	TET-5'-cacttgctgctcatctgcacag-3'-TAMRA	26	365	510
Reverse	5'-aggggatcagtaaccacaatgt-3'	22	393	511

Table BRB. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3346, Run 215601952	Tissue Name	Rel. Exp.(%) Ag3346, Run 215601952
Adipose	0.0	Renal ca. TK-10	0.0
Melanoma* Hs688(A).T	0.0	Bladder	4.7
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	4.5	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	0.0
Squamous cell carcinoma SCC-4	0.0	Colon ca. * (SW480 met) SW620	0.0
Testis Pool	6.1	Colon ca. HT29	0.0
Prostate ca. * (bone met) PC-3	0.0	Colon ca. HCT-116	0.0
Prostate Pool	0.0	Colon ca. CaCo-2	0.0
Placenta	0.0	Colon cancer tissue	0.0
Uterus Pool	0.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	0.0	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	0.0	Colon Pool	8.4
Ovarian ca. OVCAR-5	7.9	Small Intestine Pool	0.0
Ovarian ca. IGROV-1	0.0	Stomach Pool	0.0
Ovarian ca. OVCAR-8	0.0	Bone Marrow Pool	2.4
Ovary	0.0	Fetal Heart	0.0
Breast ca. MCF-7	0.0	Heart Pool	0.0
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	0.0
Breast ca. BT 549	0.0	Fetal Skeletal Muscle	0.0
Breast ca. T47D	0.0	Skeletal Muscle Pool	0.0
Breast ca. MDA-N	0.0	Spleen Pool	0.0
Breast Pool	0.0	Thymus Pool	0.0
Trachea	0.0	CNS cancer (glio/astro) U87-MG	0.0
Lung	0.0	CNS cancer (glio/astro) U-118-MG	6.0
Fetal Lung	0.0	CNS cancer (neuro;met) SK-N-AS	0.0
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	0.0	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	23.0	CNS cancer (glio) SNB-19	0.0
Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	0.0
Lung ca. A549	0.0	Brain (Amygdala) Pool	0.0
Lung ca. NCI-H526	0.0	Brain (cerebellum)	0.0
Lung ca. NCI-H23	100.0	Brain (fetal)	0.0
Lung ca. NCI-H460	19.8	Brain (Hippocampus) Pool	8.7
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	11.5
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	0.0
Liver	0.0	Brain (Thalamus) Pool	0.0
Fetal Liver	0.0	Brain (whole)	0.0
Liver ca. HepG2	0.0	Spinal Cord Pool	0.0

Kidney Pool	6.3	Adrenal Gland	0.0
Fetal Kidney	7.6	Pituitary gland Pool	0.0
Renal ca. 786-0	0.0	Salivary Gland	0.0
Renal ca. A498	0.0	Thyroid (female)	0.0
Renal ca. ACHN	4.2	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.0	Pancreas Pool	0.0

CNS_neurodegeneration_v1.0 Summary: Ag3346 Results from one experiment with the CG57845-01 gene are not included. The amp plot indicates that there were experimental difficulties with this run.

General_screening_panel_v1.4 Summary: Ag3346 Significant expression of the CG57845-01 gene is detected exclusively in a lung cancer cell line NCI-H23 sample (CT=33.7). Therefore, expression of this gene may be used to distinguish lung cancers from the other samples on this panel. Furthermore, therapeutic modulation of the activity of the GPCR encoded by this gene may be beneficial in the treatment of lung cancer.

Panel 4D Summary: Ag3346 Expression of the CG57845-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV83

Expression of NOV83 CG57843-01 was assessed using the primer-probe set Ag3345, described in Table BSA. Results of the RTQ-PCR runs are shown in Table BSB.

Table BSA. Probe Name Ag3345

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-catctccatcgacaggtacat-3'	22	379	512
Probe	TET-5'-ccctggctctctaccaagttcaccg-3'-TAMRA	27	414	513
Reverse	5'-gatgcaaattcctgacacagat-3'	22	442	514

15 Table BSB. General screening panel v1.4

Tissue Name	Rel. Exp.(%) Ag3345, Run 215773854	Tissue Name	Rel. Exp.(%) Ag3345, Run 215773854
Adipose	0.0	Renal ca. TK-10	0.0
Melanoma* Hs688(A).T	0.0	Bladder	0.0
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	0.0
Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	0.0	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	0.0
Squamous cell carcinoma SCC-4	0.0	Colon ca. * (SW480 met) SW620	0.0
Testis Pool	0.0	Colon ca. HT29	0.0
Prostate ca. * (bone met) PC-3	0.0	Colon ca. HCT-116	0.0
Prostate Pool	0.0	Colon ca. CaCo-2	0.0
Placenta	0.0	Colon cancer tissue	0.0

Uterus Pool	100.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	0.0	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	0.0	Colon Pool	0.1
Ovarian ca. OVCAR-5	0.0	Small Intestine Pool	0.0
Ovarian ca. IGROV-1	0.0	Stomach Pool	0.0
Ovarian ca. OVCAR-8	0.0	Bone Marrow Pool	0.0
Ovary	0.0	Fetal Heart	0.0
Breast ca. MCF-7	0.0	Heart Pool	0.0
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	0.0
Breast ca. BT 549	0.0	Fetal Skeletal Muscle	0.0
Breast ca. T47D	0.0	Skeletal Muscle Pool	0.0
Breast ca. MDA-N	0.0	Spleen Pool	0.0
Breast Pool	0.0	Thymus Pool	0.1
Trachea	0.0	CNS cancer (glio/astro) U87-MG	0.0
Lung	0.0	CNS cancer (glio/astro) U-118-MG	0.1
Fetal Lung	0.0	CNS cancer (neuro;met) SK-N-AS	0.0
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	0.0	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	0.2	CNS cancer (glio) SNB-19	0.0
Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	0.0
Lung ca. A549	0.0	Brain (Amygdala) Pool	0.1
Lung ca. NCI-H526	0.0	Brain (cerebellum)	0.0
Lung ca. NCI-H23	0.8	Brain (fetal)	0.0
Lung ca. NCI-H460	0.3	Brain (Hippocampus) Pool	0.0
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	0.1
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	0.1
Liver	0.0	Brain (Thalamus) Pool	0.1
Fetal Liver	3.1	Brain (whole)	0.1
Liver ca. HepG2	0.0	Spinal Cord Pool	0.0
Kidney Pool	0.1	Adrenal Gland	0.0
Fetal Kidney	0.2	Pituitary gland Pool	0.0
Renal ca. 786-0	0.0	Salivary Gland	0.0
Renal ca. A498	0.0	Thyroid (female)	0.0
Renal ca. ACHN	0.1	Pancreatic ca. CAPAN2	0.0
Renal ca. UO-31	0.0	Pancreas Pool	0.0

CNS_neurodegeneration_v1.0 Summary: Ag3345 Expression of the CG57843-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3345 Expression of the CG57843-01 gene is highest in a sample derived from normal uterus (CT = 26.6). Thus, expression of this gene can be used to distinguish uterus from the other samples on this panel. Interestingly, expression of this gene is also detected in fetal liver (CT = 31) at much higher levels than in adult liver (CT = 40), suggesting that expression of this gene can be used to distinguish fetal from adult liver.

Panel 4D Summary: Ag3345 Expression of the CG57843-01 gene is low/undetectable (CTs > 34.5) across all of the samples on this panel (data not shown).

NOV84

Expression of NOV84a, NOV84b, and NOV84c (CG57841-01, CG57841-02, and CG57837-01) was assessed using the primer-probe sets Ag3342 and Ag3344, described in Tables BTA and BTB. Results of the RTQ-PCR runs are shown in Table BTC. Please note that CG57841-02 represents a full-length physical clone of the CG57841-01 gene, validating the prediction of the gene sequence.

Table BTA. Probe Name Ag3342

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ttacctctgaccataatggaa-3'	22	111	515
Probe	TET-5'-aacctgatgctgctgctcatgatcag-3'-TAMRA	26	133	516
Reverse	5'-tacatgggcttatggagacaag-3'	22	167	517

Table BTB. Probe Name Ag3344

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ttacctctgaccataatggaa-3'	22	111	518
Probe	TET-5'-aacctgatgctgctgctcatgatcag-3'-TAMRA	26	133	519
Reverse	5'-tacatgggcttatggagacaag-3'	22	167	520

Table BTC. General_screening_panel_v1.4

Tissue Name	Rel. Exp.(%) Ag3342, Run 215773812	Tissue Name	Rel. Exp.(%) Ag3342, Run 215773812
Adipose	2.4	Renal ca. TK-10	5.3
Melanoma* Hs688(A).T	0.0	Bladder	8.3
Melanoma* Hs688(B).T	0.0	Gastric ca. (liver met.) NCI-N87	40.9
Melanoma* M14	0.0	Gastric ca. KATO III	0.0
Melanoma* LOXIMVI	4.6	Colon ca. SW-948	0.0
Melanoma* SK-MEL-5	0.0	Colon ca. SW480	7.8
Squamous cell carcinoma SCC-4	0.0	Colon ca.* (SW480 met) SW620	5.1
Testis Pool	27.4	Colon ca. HT29	0.0
Prostate ca.* (bone met) PC-3	0.0	Colon ca. HCT-116	2.3
Prostate Pool	3.4	Colon ca. CaCo-2	16.4
Placenta	0.0	Colon cancer tissue	0.0
Uterus Pool	0.0	Colon ca. SW1116	0.0
Ovarian ca. OVCAR-3	0.0	Colon ca. Colo-205	0.0
Ovarian ca. SK-OV-3	0.0	Colon ca. SW-48	0.0
Ovarian ca. OVCAR-4	4.8	Colon Pool	18.6
Ovarian ca. OVCAR-5	0.0	Small Intestine Pool	15.4
Ovarian ca. IGROV-1	4.3	Stomach Pool	0.0
Ovarian ca. OVCAR-8	0.0	Bone Marrow Pool	9.2
Ovary	21.0	Fetal Heart	0.0
Breast ca. MCF-7	7.5	Heart Pool	4.4
Breast ca. MDA-MB-231	0.0	Lymph Node Pool	21.5

Breast ca. BT 549	11.0	Fetal Skeletal Muscle	0.0
Breast ca. T47D	0.0	Skeletal Muscle Pool	3.0
Breast ca. MDA-N	0.0	Spleen Pool	5.6
Breast Pool	11.4	Thymus Pool	0.0
Trachea	0.0	CNS cancer (glio/astro) U87-MG	4.2
Lung	16.8	CNS cancer (glio/astro) U-118-MG	0.0
Fetal Lung	0.0	CNS cancer (neuro;met) SK-N-AS	0.0
Lung ca. NCI-N417	0.0	CNS cancer (astro) SF-539	0.0
Lung ca. LX-1	3.1	CNS cancer (astro) SNB-75	0.0
Lung ca. NCI-H146	12.5	CNS cancer (glio) SNB-19	0.0
Lung ca. SHP-77	0.0	CNS cancer (glio) SF-295	5.4
Lung ca. A549	0.0	Brain (Amygdala) Pool	0.0
Lung ca. NCI-H526	0.0	Brain (cerebellum)	5.9
Lung ca. NCI-H23	100.0	Brain (fetal)	0.0
Lung ca. NCI-H460	8.3	Brain (Hippocampus) Pool	15.3
Lung ca. HOP-62	0.0	Cerebral Cortex Pool	8.1
Lung ca. NCI-H522	0.0	Brain (Substantia nigra) Pool	7.7
Liver	0.0	Brain (Thalamus) Pool	11.0
Fetal Liver	0.0	Brain (whole)	0.0
Liver ca. HepG2	0.0	Spinal Cord Pool	16.4
Kidney Pool	23.8	Adrenal Gland	4.6
Fetal Kidney	15.7	Pituitary gland Pool	0.0
Renal ca. 786-0	4.7	Salivary Gland	4.8
Renal ca. A498	0.0	Thyroid (female)	0.0
Renal ca. ACHN	0.0	Pancreatic ca. CAPAN2	9.8
Renal ca. UO-31	0.0	Pancreas Pool	13.7

CNS_neurodegeneration_v1.0 Summary: Ag3342/Ag3344 Expression of the CG57841-01 gene is low/undetectable (CTs > 34.5) across all of the samples on this panel (data not shown).

General_screening_panel_v1.4 Summary: Ag3342 Significant expression of the CG57841-01 gene is seen exclusively in a lung cancer NCI-H23 sample (CT = 34.1). Therefore, expression of this gene may be used to distinguish this sample from the other samples on this panel. Furthermore, therapeutic modulation of the activity of the GPCR encoded by this gene may be beneficial in the treatment of lung cancer. Ag3344 Results from one experiment with the CG57841-01 gene are not included. The amp plot indicates that there were experimental difficulties with this run.

Panel 4D Summary: Ag3342/Ag3344 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV85

Tissue Name	Rel. Exp.(%) Ag2308, Run 158927487	Tissue Name	Rel. Exp.(%) Ag2308, Run 158927487
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	17.4
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	17.2	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	4.4
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	11.3	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	24.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	14.5	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	15.1
CD45RA CD4 lymphocyte act	0.0	Coronary artery SMC rest	0.0
CD45RO CD4 lymphocyte act	6.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	0.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	0.0	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	29.1
LAK cells IL-2+IL-12	0.0	Lupus kidney	9.9
LAK cells IL-2+IFN gamma	21.8	NCI-H292 none	26.6
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	28.7
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	37.9
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	10.6	NCI-H292 IFN gamma	13.3
Two Way MLR 5 day	21.5	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	0.0
PBMC rest	0.0	Lung fibroblast none	11.3
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	14.6	Lung fibroblast IL-4	18.6
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	15.9
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	22.2
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	0.0	Dermal fibroblast CCD1070 TNF alpha	6.7
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	0.0	Dermal fibroblast IFN gamma	0.0

A2A receptor antagonists in reducing immobility time in the tail suspension test was confirmed and extended in two groups of mice. Specifically, SCH 58261 (1 - 10 mg kg⁻¹) and ZM 241385 (15 - 60 mg kg⁻¹) were effective in mice previously screened for having high immobility time, while SCH 58261 at 10 mg kg⁻¹ reduced immobility of mice that were selectively bred for their spontaneous 'helplessness' in this assay. 5. Additional experiments were carried out using the forced swim test. SCH 58261 at 10 mg kg⁻¹ reduced the immobility time by 61%, while KW 6002 decreased the total immobility time at the doses of 1 and 10 mg kg⁻¹ by 75 and 79%, respectively. 6. Administration of the dopamine D2 receptor antagonist haloperidol (50 - 200 microg kg⁻¹ i.p.) prevented the antidepressant-like effects elicited by SCH 58261 (10 mg kg⁻¹ i.p.) in forced swim test whereas it left unaltered its stimulant motor effects. 7. In conclusion, these data support the hypothesis that A2A receptor antagonists prolong escape-directed behaviour in two screening tests for antidepressants. Altogether the results support the hypothesis that blockade of the adenosine A2A receptor might be an interesting target for the development of effective antidepressant agents.

2. Blier P. Pharmacology of rapid-onset antidepressant treatment strategies. Clin Psychiatry 2001;62 Suppl 15:12-7

Although selective serotonin reuptake inhibitors (SSRIs) block serotonin (5-HT) reuptake rapidly, their therapeutic action is delayed. The increase in synaptic 5-HT activates feedback mechanisms mediated by 5-HT_{1A} (cell body) and 5-HT_{1B} (terminal) autoreceptors, which, respectively, reduce the firing in 5-HT neurons and decrease the amount of 5-HT released per action potential resulting in attenuated 5-HT neurotransmission. Long-term treatment desensitizes the inhibitory 5-HT₁ autoreceptors, and 5-HT neurotransmission is enhanced. The time course of these events is similar to the delay of clinical action. The addition of pindolol, which blocks 5-HT_{1A} receptors, to SSRI treatment decouples the feedback inhibition of 5-HT neuron firing and accelerates and enhances the antidepressant response. The neuronal circuitry of the 5-HT and norepinephrine (NE) systems and their connections to forebrain areas believed to be involved in depression has been dissected. The firing of 5-HT neurons in the raphe nuclei is driven, at least partly, by alpha₁-adrenoceptor-mediated excitatory inputs from NE neurons. Inhibitory alpha₂-adrenoceptors on the NE neuroterminals form part of a feedback control mechanism. Mirtazapine, an antagonist at alpha₂-adrenoceptors, does not enhance 5-HT neurotransmission directly but disinhibits the NE activation of 5-HT neurons and thereby increases 5-HT neurotransmission by a mechanism that does not require a time-dependent desensitization of receptors. These

neurobiological phenomena may underlie the apparently faster onset of action of mirtazapine compared with the SSRIs.

3. Tranquillini ME, Reggiani A. Glycine-site antagonists and stroke. *Expert Opin Investig Drugs* 1999 Nov;8(11):1837-1848

5 The excitatory amino acid, (S)-glutamic acid, plays an important role in controlling many neuronal processes. Its action is mediated by two main groups of receptors: the ionotropic receptors (which include NMDA, AMPA and kainic acid subtypes) and the metabotropic receptors (mGluR(1-8)) mediating G-protein coupled responses. This review focuses on the strychnine insensitive glycine binding site located on the NMDA receptor
10 channel, and on the possible use of selective antagonists for the treatment of stroke. Stroke is a devastating disease caused by a sudden vascular accident. Neurochemically, a massive release of glutamate occurs in neuronal tissue; this overactivates the NMDA receptor, leading to increased intracellular calcium influx, which causes neuronal cell death through necrosis. NMDA receptor activation strongly depends upon the presence of glycine as a co-agonist.
15 Therefore, the administration of a glycine antagonist can block overactivation of NMDA receptors, thus preserving neurones from damage. The glycine antagonists currently identified can be divided into five main categories depending on their chemical structure: indoles, tetrahydroquinolines, benzoazepines, quinoxalinediones and pyrida-zinoquinolines.

4. Monopoli A, Lozza G, Forlani A, Mattavelli A, Ongini E. Blockade of adenosine
20 A2A receptors by SCH 58261 results in neuroprotective effects in cerebral ischaemia in rats. *Neuroreport* 1998 Dec 1;9(17):3955-9

 Blockade of adenosine receptors can reduce cerebral infarct size in the model of global ischaemia. Using the potent and selective A2A adenosine receptor antagonist, SCH 58261, we assessed whether A2A receptors are involved in the neuronal damage following focal cerebral
25 ischaemia as induced by occluding the left middle cerebral artery. SCH 58261 (0.01 mg/kg either i.p. or i.v.) administered to normotensive rats 10 min after ischaemia markedly reduced cortical infarct volume as measured 24 h later (30% vs controls, $p < 0.05$). Similar effects were observed when SCH 58261 (0.01 mg/kg, i.p.) was administered to hypertensive rats (28% infarct volume reduction vs controls, $p < 0.05$). Neuroprotective properties of SCH 58261
30 administered after ischaemia indicate that blockade of A2A adenosine receptors is a potentially useful biological target for the reduction of brain injury.

Panel 1.3D Summary: Ag2308 Expression of the CG57839-01 gene is low/undetectable (CT>35) in all samples shown in this Panel (data not shown).

Panel 4D Summary: Ag2308 Expression of the CG57839-01 gene is detected in the thymus (CT = 33.3) and lung (CT = 34.4). Thus, expression of this gene could be used as a marker to detect the presence of thymus or lung tissue. The putative GPCR encoded for by this gene may also play an important role in the normal homeostasis of these tissues. Therefore, therapeutics designed with this gene product could be important for maintaining or restoring normal function to these organs during inflammation. Ag3343 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

NOV87

Expression of NOV87 CG56763-01 was assessed using the primer-probe set Ag3012, described in Table BVA. Results of the RTQ-PCR runs are shown in Tables BVB, and BVC.

Table BVA. Probe Name Ag3012

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-ctctttgtcctggaggagaac-3'	21	162	527
Probe	TET-5'-acctccctccacaggcccatgtacta-3'-TAMRA	26	213	528
Reverse	5'-gaaagacatggagctcagaaag-3'	22	239	529

Table BVB. Panel 1.3D

Tissue Name	Rel. Exp.(%) Ag3012, Run 167810404	Tissue Name	Rel. Exp.(%) Ag3012, Run 167810404
Liver adenocarcinoma	0.0	Kidney (fetal)	0.0
Pancreas	0.0	Renal ca. 786-0	0.0
Pancreatic ca. CAPAN 2	1.6	Renal ca. A498	0.0
Adrenal gland	0.0	Renal ca. RXF 393	0.0
Thyroid	0.0	Renal ca. ACHN	0.0
Salivary gland	2.8	Renal ca. UO-31	0.0
Pituitary gland	0.0	Renal ca. TK-10	0.0
Brain (fetal)	0.0	Liver	0.0
Brain (whole)	0.0	Liver (fetal)	0.0
Brain (amygdala)	12.6	Liver ca. (hepatoblast) HepG2	0.0
Brain (cerebellum)	0.0	Lung	0.0
Brain (hippocampus)	5.5	Lung (fetal)	0.0
Brain (substantia nigra)	3.0	Lung ca. (small cell) LX-1	1.4
Brain (thalamus)	3.1	Lung ca. (small cell) NCI-H69	0.0
Cerebral Cortex	0.0	Lung ca. (s.cell var.) SHP-77	2.4
Spinal cord	100.0	Lung ca. (large cell) NCI-H460	0.0
glio/astro U87-MG	0.0	Lung ca. (non-sm. cell) A549	0.0
glio/astro U-118-MG	0.0	Lung ca. (non-s.cell) NCI-H23	0.0
astrocytoma SW1783	0.0	Lung ca. (non-s.cell) HOP-62	0.0
neuro*; met SK-N-AS	0.0	Lung ca. (non-s.cl) NCI-	0.0

		H522	
astrocytoma SF-539	0.0	Lung ca. (squam.) SW 900	0.0
astrocytoma SNB-75	0.0	Lung ca. (squam.) NCI-H596	0.0
glioma SNB-19	3.2	Mammary gland	2.9
glioma U251	0.0	Breast ca.* (pl.ef) MCF-7	3.5
glioma SF-295	0.0	Breast ca.* (pl.ef) MDA-MB-231	0.0
Heart (fetal)	0.0	Breast ca.* (pl.ef) T47D	0.0
Heart	2.6	Breast ca. BT-549	0.0
Skeletal muscle (fetal)	12.5	Breast ca. MDA-N	0.0
Skeletal muscle	0.0	Ovary	0.0
Bone marrow	0.0	Ovarian ca. OVCAR-3	3.0
Thymus	9.5	Ovarian ca. OVCAR-4	0.0
Spleen	0.0	Ovarian ca. OVCAR-5	3.5
Lymph node	0.0	Ovarian ca. OVCAR-8	0.0
Colorectal	4.3	Ovarian ca. IGROV-1	0.0
Stomach	0.0	Ovarian ca.* (ascites) SK-OV-3	0.0
Small intestine	0.0	Uterus	0.0
Colon ca. SW480	0.0	Placenta	0.0
Colon ca.* SW620(SW480 met)	0.0	Prostate	0.0
Colon ca. HT29	0.0	Prostate ca.* (bone met)PC-3	0.0
Colon ca. HCT-116	0.0	Testis	35.4
Colon ca. CaCo-2	0.0	Melanoma Hs688(A).T	0.0
Colon ca. tissue(ODO3866)	0.0	Melanoma* (met) Hs688(B).T	0.0
Colon ca. HCC-2998	6.0	Melanoma UACC-62	0.0
Gastric ca.* (liver met) NCI-N87	0.0	Melanoma M14	0.0
Bladder	0.0	Melanoma LOX IMVI	0.0
Trachea	0.0	Melanoma* (met) SK-MEL-5	0.0
Kidney	0.0	Adipose	0.0

Table BVC. Panel 4D

Tissue Name	Rel. Exp.(%) Ag3012, Run 164404080	Tissue Name	Rel. Exp.(%) Ag3012, Run 164404080
Secondary Th1 act	0.0	HUVEC IL-1beta	0.0
Secondary Th2 act	0.0	HUVEC IFN gamma	0.0
Secondary Tr1 act	0.0	HUVEC TNF alpha + IFN gamma	0.0
Secondary Th1 rest	0.0	HUVEC TNF alpha + IL4	0.0
Secondary Th2 rest	0.0	HUVEC IL-11	0.0
Secondary Tr1 rest	0.0	Lung Microvascular EC none	0.0
Primary Th1 act	0.0	Lung Microvascular EC TNFalpha + IL-1beta	0.0
Primary Th2 act	0.0	Microvascular Dermal EC none	0.0
Primary Tr1 act	0.0	Microvascular Dermal EC TNFalpha + IL-1beta	0.0
Primary Th1 rest	0.0	Bronchial epithelium TNFalpha + IL1beta	0.0
Primary Th2 rest	8.0	Small airway epithelium none	0.0
Primary Tr1 rest	0.0	Small airway epithelium TNFalpha + IL-1beta	0.0

Panel 1.3D Summary: Ag3012 The CG56763-01 gene is expressed at low levels in the samples derived from spinal cord (CT = 32.1) and testis (CT=33.6). Thus, the expression of this gene could be used to distinguish these samples from the other samples in the panel.

CD45RO CD4 lymphocyte act	0.0	Coronary artery SMC TNFalpha + IL-1beta	0.0
CD8 lymphocyte act	0.0	Astrocytes rest	0.0
Secondary CD8 lymphocyte rest	0.0	Astrocytes TNFalpha + IL-1beta	0.0
Secondary CD8 lymphocyte act	0.0	KU-812 (Basophil) rest	0.0
CD4 lymphocyte none	0.0	KU-812 (Basophil) PMA/ionomycin	24.0
2ry Th1/Th2/Tr1_anti-CD95 CH11	5.1	CCD1106 (Keratinocytes) none	0.0
LAK cells rest	0.0	CCD1106 (Keratinocytes) TNFalpha + IL-1beta	0.0
LAK cells IL-2	0.0	Liver cirrhosis	72.2
LAK cells IL-2+IL-12	0.0	Lupus kidney	0.0
LAK cells IL-2+IFN gamma	0.0	NCI-H292 none	20.7
LAK cells IL-2+ IL-18	0.0	NCI-H292 IL-4	0.0
LAK cells PMA/ionomycin	0.0	NCI-H292 IL-9	0.0
NK Cells IL-2 rest	0.0	NCI-H292 IL-13	0.0
Two Way MLR 3 day	0.0	NCI-H292 IFN gamma	0.0
Two Way MLR 5 day	0.0	HPAEC none	0.0
Two Way MLR 7 day	0.0	HPAEC TNF alpha + IL-1 beta	1.4
PBMC rest	0.0	Lung fibroblast none	0.0
PBMC PWM	0.0	Lung fibroblast TNF alpha + IL-1 beta	0.0
PBMC PHA-L	0.0	Lung fibroblast IL-4	0.0
Ramos (B cell) none	0.0	Lung fibroblast IL-9	0.0
Ramos (B cell) ionomycin	0.0	Lung fibroblast IL-13	0.0
B lymphocytes PWM	0.0	Lung fibroblast IFN gamma	3.2
B lymphocytes CD40L and IL-4	0.0	Dermal fibroblast CCD1070 rest	0.0
EOL-1 dbcAMP	3.1	Dermal fibroblast CCD1070 TNF alpha	0.0
EOL-1 dbcAMP PMA/ionomycin	0.0	Dermal fibroblast CCD1070 IL-1 beta	0.0
Dendritic cells none	33.2	Dermal fibroblast IFN gamma	0.0
Dendritic cells LPS	2.4	Dermal fibroblast IL-4	1.9
Dendritic cells anti-CD40	100.0	IBD Colitis 2	16.3
Monocytes rest	0.0	IBD Crohn's	6.7
Monocytes LPS	0.0	Colon	0.0
Macrophages rest	44.1	Lung	21.8
Macrophages LPS	0.0	Thymus	0.0
HUVEC none	3.1	Kidney	0.0
HUVEC starved	0.0		

Panel 1.3D Summary: Ag2875/Ag3010 Results from two experiments with the CG56753-01 gene are not included. The amp plots indicate that there were experimental difficulties with these runs.

Panel 2.2 Summary: Ag2875 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gtccttgaaggatccaaaactc-3'	22	162	539
Probe	TET-5'-tttcttcttccaaccttccctgg-3'-TAMRA	26	198	540
Reverse	5'-ctgctgggtcaaacagagggtcta-3'	22	224	541

Table BYB. Probe Name Ag3306

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-gggcaaatttctcactcttttc-3'	22	828	542
Probe	TET-5'-ccccaaactttaatccctcatctaca-3'-TAMRA	27	863	543
Reverse	5'-ccctttacctcctgttcctta-3'	22	893	544

Table BYC. Probe Name Gpcr22

Primers	Sequences	Length	Start Position	SEQ ID NO
Forward	5'-aattcagatgtctatgccagtgtt-3'	25	606	545
Probe	TET-5'-tcctcctggtgatgcccttgatcattatc-3'-TAMRA	29	632	546
Reverse	5'-tagcaatagcaccagaagaggaaa-3'	25	662	547

Table BYD. CNS_neurodegeneration_v1.0

Tissue Name	Rel. Exp.(%) Ag2497, Run 208122050	Tissue Name	Rel. Exp.(%) Ag2497, Run 208122050
AD 1 Hippo	16.4	Control (Path) 3 Temporal Ctx	0.0
AD 2 Hippo	20.6	Control (Path) 4 Temporal Ctx	0.0
AD 3 Hippo	22.8	AD 1 Occipital Ctx	0.0
AD 4 Hippo	0.0	AD 2 Occipital Ctx (Missing)	0.0
AD 5 Hippo	0.0	AD 3 Occipital Ctx	0.0
AD 6 Hippo	87.1	AD 4 Occipital Ctx	0.0
Control 2 Hippo	6.2	AD 5 Occipital Ctx	0.0
Control 4 Hippo	30.6	AD 6 Occipital Ctx	0.0
Control (Path) 3 Hippo	25.0	Control 1 Occipital Ctx	0.0
AD 1 Temporal Ctx	0.0	Control 2 Occipital Ctx	0.0
AD 2 Temporal Ctx	6.9	Control 3 Occipital Ctx	0.0
AD 3 Temporal Ctx	0.0	Control 4 Occipital Ctx	0.0
AD 4 Temporal Ctx	0.0	Control (Path) 1 Occipital Ctx	5.6
AD 5 Inf Temporal Ctx	0.0	Control (Path) 2 Occipital Ctx	0.0
AD 5 Sup Temporal Ctx	100.0	Control (Path) 3 Occipital Ctx	0.0
AD 6 Inf Temporal Ctx	0.0	Control (Path) 4 Occipital Ctx	0.0
AD 6 Sup Temporal Ctx	0.0	Control 1 Parietal Ctx	0.0
Control 1 Temporal Ctx	0.0	Control 2 Parietal Ctx	0.0
Control 2 Temporal Ctx	0.0	Control 3 Parietal Ctx	0.0
Control 3 Temporal Ctx	0.0	Control (Path) 1 Parietal Ctx	0.0
Control 3 Temporal Ctx	0.0	Control (Path) 2 Parietal Ctx	0.0
Control (Path) 1 Temporal Ctx	0.0	Control (Path) 3 Parietal Ctx	0.0
Control (Path) 2 Temporal Ctx	0.0	Control (Path) 4 Parietal Ctx	0.0

Table BYE. Panel 1.1

Tissue Name	Tissue Name
-------------	-------------

	109664919		109664919
Adrenal gland	0.0	Renal ca. UO-31	7.9
Bladder	2.3	Renal ca. RXF 393	0.0
Brain (amygdala)	0.0	Liver	0.0
Brain (cerebellum)	0.1	Liver (fetal)	5.3
Brain (hippocampus)	0.0	Liver ca. (hepatoblast) HepG2	0.0
Brain (substantia nigra)	6.9	Lung	0.1
Brain (thalamus)	7.2	Lung (fetal)	0.6
Cerebral Cortex	1.0	Lung ca. (non-s.cell) HOP-62	18.4
Brain (fetal)	0.1	Lung ca. (large cell) NCI-H460	0.0
Brain (whole)	0.1	Lung ca. (non-s.cell) NCI-H23	18.2
glio/astro U-118-MG	0.0	Lung ca. (non-s.cl) NCI-H522	16.4
astrocytoma SF-539	0.7	Lung ca. (non-sm. cell) A549	8.6
astrocytoma SNB-75	0.0	Lung ca. (s.cell var.) SHP-77	1.0
astrocytoma SW1783	0.0	Lung ca. (small cell) LX-1	0.0
glioma U251	0.0	Lung ca. (small cell) NCI-H69	57.4
glioma SF-295	0.0	Lung ca. (squam.) SW 900	4.3
glioma SNB-19	10.7	Lung ca. (squam.) NCI-H596	9.2
glio/astro U87-MG	0.0	Lymph node	0.0
neuro*; met SK-N-AS	0.0	Spleen	0.0
Mammary gland	0.1	Thymus	0.5
Breast ca. BT-549	1.8	Ovary	6.6
Breast ca. MDA-N	1.1	Ovarian ca. IGROV-1	0.5
Breast ca. * (pl.ef) T47D	25.7	Ovarian ca. OVCAR-3	14.2
Breast ca. * (pl.ef) MCF-7	2.5	Ovarian ca. OVCAR-4	3.2
Breast ca. * (pl.ef) MDA-MB-231	0.0	Ovarian ca. OVCAR-5	51.1
Small intestine	0.0	Ovarian ca. OVCAR-8	6.3
Colorectal	4.0	Ovarian ca. * (ascites) SK-OV-3	62.4
Colon ca. HT29	5.7	Pancreas	4.5
Colon ca. CaCo-2	2.3	Pancreatic ca. CAPAN 2	0.0
Colon ca. HCT-15	12.2	Pituitary gland	3.7
Colon ca. HCT-116	0.0	Placenta	0.0
Colon ca. HCC-2998	1.3	Prostate	0.0
Colon ca. SW480	0.8	Prostate ca. * (bone met) PC-3	0.5
Colon ca. * SW620 (SW480 met)	0.0	Salivary gland	0.6
Stomach	0.0	Trachea	0.0
Gastric ca. (liver met) NCI-N87	8.2	Spinal cord	10.4
Heart	0.0	Testis	100.0
Skeletal muscle (Fetal)	0.3	Thyroid	0.0
Skeletal muscle	0.4	Uterus	0.0
Endothelial cells	0.1	Melanoma M14	8.4
Heart (Fetal)	0.3	Melanoma LOX IMVI	0.0

Kidney	0.3	Melanoma UACC-62	0.0
Kidney (fetal)	0.0	Melanoma SK-MEL-28	1.0
Renal ca. 786-0	2.3	Melanoma* (met) SK-MEL-5	0.0
Renal ca. A498	1.1	Melanoma Hs688(A).T	0.0
Renal ca. ACHN	0.0	Melanoma* (met) Hs688(B).T	0.5
Renal ca. TK-10	0.2		

CNS_neurodegeneration_v1.0 Summary: Ag2497 A low level of expression of the CG57678-01 gene is detected with samples derived from one of the Alzheimer's patient hippocampus (CT=34.3) and sup temporal cortex (CT=34.1). Therefore, expression of this gene may be used to distinguish these samples from the other samples on this panel. This gene
5 encodes a putative GPCR; therefore, therapeutic modulation of this gene or its protein product may be beneficial in the treatment of one or more of CNS disorders, as may stimulation and/or blockade of the receptor coded for by the gene.

Ag3306 Expression of this gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

10 **General_screening_panel_v1.4 Summary:** Ag3306 Expression of the CG57678-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 1.1 Summary: Gpcr22 Expression of the CG57678-01 gene is highest in testis (CT = 29.2). In addition, this gene is expressed at significant levels in some regions of the central nervous system, including spinal cord, substantia nigra and thalamus. The CG57678-01
15 gene encodes a putative GPCR. Several neurotransmitter receptors are GPCRs, including the dopamine receptor family, the serotonin receptor family, the GABAB receptor, muscarinic acetylcholine receptors, and others; thus this GPCR may represent a novel neurotransmitter receptor. Targeting various neurotransmitter receptors (dopamine, serotonin) has proven to be an effective therapy in psychiatric illnesses such as schizophrenia, bipolar disorder, and
20 depression. Furthermore, the cerebral cortex and hippocampus are regions of the brain that are known to be involved in Alzheimer's disease, seizure disorders, and in the normal process of memory formation. Therefore, therapeutic modulation of this gene or its protein product may be beneficial in the treatment of one or more of these diseases, as may stimulation and/or blockade of the receptor coded for by the gene.

25 In addition, expression of this gene is upregulated in a number of lung cancer cell lines compared to normal lung. Therefore, therapeutic modulation of the activity of this gene or its protein product, using small molecule drugs, antibodies or protein therapeutics, may be of benefit in the treatment of lung cancer.

Panel 1.3D Summary: Ag2497 Expression of the CG57678-01 gene is low/undetectable (CTs > 35) across all of the samples on this panel (data not shown).

Panel 2.2 Summary: Ag2497 Expression of the CG57678-01 gene is low/undetectable (CTs > 34.5) across all of the samples on this panel (data not shown).

5 **Panel 4D Summary:** Ag2497 Expression of the CG57678-01 gene is low/undetectable (CTs > 34.5) across all of the samples on this panel (data not shown).

Example 3. SNP analysis of NOVX clones

SeqCalling™ Technology: cDNA was derived from various human samples representing multiple tissue types, normal and diseased states, physiological states, and developmental states from different donors. Samples were obtained as whole tissue, cell lines, primary cells or tissue cultured primary cells and cell lines. Cells and cell lines may have been treated with biological or chemical agents that regulate gene expression for example, growth factors, chemokines, steroids. The cDNA thus derived was then sequenced using CuraGen's proprietary SeqCalling technology. Sequence traces were evaluated manually and edited for corrections if appropriate. cDNA sequences from all samples were assembled with themselves and with public ESTs using bioinformatics programs to generate CuraGen's human SeqCalling database of SeqCalling assemblies. Each assembly contains one or more overlapping cDNA sequences derived from one or more human samples. Fragments and ESTs were included as components for an assembly when the extent of identity with another component of the assembly was at least 95% over 50 bp. Each assembly can represent a gene and/or its variants such as splice forms and/or single nucleotide polymorphisms (SNPs) and their combinations.

Variant sequences are included in this application. A variant sequence can include a single nucleotide polymorphism (SNP). A SNP can, in some instances, be referred to as a "cSNP" to denote that the nucleotide sequence containing the SNP originates as a cDNA. A SNP can arise in several ways. For example, a SNP may be due to a substitution of one nucleotide for another at the polymorphic site. Such a substitution can be either a transition or a transversion. A SNP can also arise from a deletion of a nucleotide or an insertion of a nucleotide, relative to a reference allele. In this case, the polymorphic site is a site at which one allele bears a gap with respect to a particular nucleotide in another allele. SNPs occurring within genes may result in an alteration of the amino acid encoded by the gene at the position of the SNP. Intragenic SNPs may also be silent, however, in the case that a codon including a SNP encodes the same amino acid as a result of the redundancy of the genetic code. SNPs occurring outside the region of a gene, or in an intron within a gene, do not result in changes in

any amino acid sequence of a protein but may result in altered regulation of the expression pattern for example, alteration in temporal expression, physiological response regulation, cell type expression regulation, intensity of expression, stability of transcribed message.

Method of novel SNP Identification: SNPs are identified by analyzing sequence assemblies using CuraGen's proprietary SNPTool algorithm. SNPTool identifies variation in assemblies with the following criteria: SNPs are not analyzed within 10 base pairs on both ends of an alignment; Window size (number of bases in a view) is 10; The allowed number of mismatches in a window is 2; Minimum SNP base quality (PHRED score) is 23; Minimum number of changes to score an SNP is 2/assembly position. SNPTool analyzes the assembly and displays SNP positions, associated individual variant sequences in the assembly, the depth of the assembly at that given position, the putative assembly allele frequency, and the SNP sequence variation. Sequence traces are then selected and brought into view for manual validation. The consensus assembly sequence is imported into CuraTools along with variant sequence changes to identify potential amino acid changes resulting from the SNP sequence variation. Comprehensive SNP data analysis is then exported into the SNPCalling database.

Method of novel SNP Confirmation: SNPs are confirmed employing a validated method known as Pyrosequencing (Pyrosequencing, Westborough, MA). Detailed protocols for Pyrosequencing can be found in: Alderborn et al. Determination of Single Nucleotide Polymorphisms by Real-time Pyrophosphate DNA Sequencing. (2000). *Genome Research*. 10, Issue 8, August. 1249-1265. In brief, Pyrosequencing is a real time primer extension process of genotyping. This protocol takes double-stranded, biotinylated PCR products from genomic DNA samples and binds them to streptavidin beads. These beads are then denatured producing single stranded bound DNA. SNPs are characterized utilizing a technique based on an indirect bioluminometric assay of pyrophosphate (PPi) that is released from each dNTP upon DNA chain elongation. Following Klenow polymerase-mediated base incorporation, PPi is released and used as a substrate, together with adenosine 5'-phosphosulfate (APS), for ATP sulfurylase, which results in the formation of ATP. Subsequently, the ATP accomplishes the conversion of luciferin to its oxi-derivative by the action of luciferase. The ensuing light output becomes proportional to the number of added bases, up to about four bases. To allow processivity of the method dNTP excess is degraded by apyrase, which is also present in the starting reaction mixture, so that only dNTPs are added to the template during the sequencing. The process has been fully automated and adapted to a 96-well format, which allows rapid screening of large SNP panels. The DNA and protein sequences for the novel single nucleotide polymorphic variants are reported. Variants are reported individually but any combination of all or a select

subset of variants are also included. In addition, the positions of the variant bases and the variant amino acid residues are underlined.

Results

5 Variants are reported individually but any combination of all or a select subset of variants are also included as contemplated NOVX embodiments of the invention.

NOV36a SNP data:

NOV36a has 4 SNP variants, whose variant positions for their nucleotide and amino acid sequences is numbered according to SEQ ID NOs:81 and 82, respectively. The nucleotide sequence of the NOV36a variants differs as shown in Table SNP1.

10

Table SNP1. cSNP and Coding Variants for NOV36a				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
284	T	C	87	Phe to Ser
307	G	A	95	Gly to Ser
354	A	G	110	Ala to Ala
379	T	C	119	Ser to Pro

NOV55 SNP data:

NOV55 has 5 SNP variants, whose variant positions for their nucleotide and amino acid sequences is numbered according to SEQ ID NOs:127 and 128, respectively. The nucleotide sequence of the NOV55 variants differs as shown in Table SNP2.

15

Table SNP2. cSNP and Coding Variants for NOV55				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
149	A	T	45	Ser to Cys
227	G	A	71	Glu to Lys
304	C	T	96	His to His
2542	T	C	842	His to His
2838	T	C	941	Ile to Thr

NOV SNP19 data:

NOV19 has one SNP variant, whose variant positions for their nucleotide and amino acid sequences is numbered according to SEQ ID NOs:47 and 48, respectively. The nucleotide sequence of the NOV19 variants differs as shown in Table SNP3.

20

Table SNP3. cSNP and Coding Variants for NOV19				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change

893	C	T	289	Ala to Val
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NOV8a SNP data:

NOV8a has two SNP variants, whose variant positions for their nucleotide and amino acid sequences is numbered according to SEQ ID NOs:17 and 18, respectively. The nucleotide sequence of the NOV8a variants differs as shown in Table SNP4.

Table SNP4. cSNP and Coding Variants for NOV8a				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
1199	T	C	380	Leu to Pro
1213	G	A	385	Gly to Ser

NOV62a SNP data:

NOV62a has three SNP variants, whose variant positions for their nucleotide and amino acid sequences is numbered according to SEQ ID NOs:145 and 156, respectively. The nucleotide sequence of the NOV62a variants differs as shown in Table SNP5.

Table SNP5. cSNP and Coding Variants for NOV62a				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
1197	G	A	366	Ala to Thr
1237	A	G	379	Asp to Gly
1285	C	T	395	Ala to Val

NOV SNP11a data:

NOV11a has four SNP variants, whose variant positions for their nucleotide and amino acid sequences is numbered according to SEQ ID NOs:25 and 26, respectively. The nucleotide sequence of the NOV11a variants differs as shown in Table SNP6.

Table SNP6. cSNP and Coding Variants for NOV11a				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
636	C	T	212	No change
1089	G	A	363	Met to Ile
5654	A	G	1885	Gln to Art
5914	C	A	0	Silent

NOV25 SNP data:

NOV25 has one SNP variant, whose variant positions for their nucleotide and amino acid sequences is numbered according to SEQ ID NOs:59 and 60, respectively. The nucleotide sequence of the NOV25 variants differs as shown in Table SNP7.

Table SNP7. cSNP and Coding Variants for NOV25				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
1836	C	T	612	No change

NOV10 SNP data:

NOV10 has one SNP variant, whose variant positions for their nucleotide and amino acid sequences is numbered according to SEQ ID NOs:23 and 24, respectively. The nucleotide sequence of the NOV10 variant differs as shown in Table SNP8.

Table SNP8. cSNP and Coding Variants for NOV10				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
715	T	C	239	Ser to Pro

NOV3 SNP data:

NOV3 has two SNP variants, whose variant positions for their nucleotide and amino acid sequences is numbered according to SEQ ID NOs:5 and 6, respectively. The nucleotide sequence of the NOV3 variants differs as shown in Table SNP9.

Table SNP9. cSNP and Coding Variants for NOV3				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
127	C	T	9	No change
158	G	A	20	Val to Met

NOV44a SNP data:

NOV44a has four SNP variants, whose variant positions for their nucleotide and amino acid sequences is numbered according to SEQ ID NOs:101 and 102, respectively. The nucleotide sequence of the NOV44a variants differs as shown in Table SNP10.

Table SNP10. cSNP and Coding Variants for NOV44a				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
56	G	T	7	Gly to Val
164	C	A	43	Pro to His

422	G	A	129	Gly to Asp
500	T	C	155	Leu to Pro

NOV57 SNP data:

- NOV57 has one SNP variant, whose variant positions for its nucleotide and amino acid sequences is numbered according to SEQ ID NOs:131 and 132, respectively. The nucleotide sequence of the NOV57 variant differs as shown in Table SNP11.

Table SNP11. cSNP and Coding Variants for NOV57				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
1214	C	T	362	No change

NOV15 SNP data:

- NOV15 has 14 SNP variants, whose variant positions for their nucleotide and amino acid sequences is numbered according to SEQ ID NOs:39 and 40, respectively. The nucleotide sequence of the NOV15 variants differs as shown in Table SNP12.

Table SNP12. cSNP and Coding Variants for NOV15				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
136	T	C	11	No change
187	T	C	28	No change
189	A	G	29	Asp to Gly
259	A	G	52	No change
266	C	T	55	Gln to stop
434	C	T	111	Pro to Ser
998	A	G	299	Ile to Val
1252	G	A	383	No change
1409	A	G	436	Thr to Ala
1428	T	C	442	Leu to Ser
1429	G	A	442	No change
1935	A	G	611	His to Arg
1967	G	T	622	Gly to Cys
2063	G	C	654	Ala to Pro

NOV21 SNP data:

- NOV21 has one SNP variant, whose variant positions for its nucleotide and amino acid sequences is numbered according to SEQ ID NOs:51 and 52, respectively. The nucleotide sequence of the NOV21 variants differs as shown in Table SNP13.

Table SNP13. cSNP and Coding Variants for NOV21				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
814	T	C	196	No change

NOV45a SNP data:

- NOV45a has one SNP variant, whose variant positions for its nucleotide and amino acid sequences is numbered according to SEQ ID NOs:105 and 106, respectively. The nucleotide sequence of the NOV45a variants differs as shown in Table SNP14.

Table SNP14. cSNP and Coding Variants for NOV45a				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
4091	A	G	1353	Thr to Ala

NOV54 SNP data:

- NOV54 has one SNP variant, whose variant positions for its nucleotide and amino acid sequences is numbered according to SEQ ID NOs:125 and 126, respectively. The nucleotide sequence of the NOV54 variants differs as shown in Table SNP15.

Table SNP15. cSNP and Coding Variants for NOV54				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
3208	C	T	Silent	No change

NOV69a SNP data:

- NOV69a has four SNP variants, whose variant positions for their nucleotide and amino acid sequences is numbered according to SEQ ID NOs:163 and 164, respectively. The nucleotide sequence of the NOV69a variants differs as shown in Table SNP16.

Table SNP16. cSNP and Coding Variants for NOV69a				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
1052	G	A	327	No change
1171	A	G	367	Lys to Arg
1186	A	G	372	Glu to Gly
1316	C	A	415	No change

NOV58 SNP data:

NOV58 has three SNP variants, whose variant positions for their nucleotide and amino acid sequences is numbered according to SEQ ID NOs:133 and 134, respectively. The nucleotide sequence of the NOV58 variants differs as shown in Table SNP17.

Table SNP17. cSNP and Coding Variants for NOV58				
NT Position of cSNP	Wild Type NT	Variant NT	Amino Acid position	Amino Acid Change
579	C	T	174	Gln to Stop
598	C	T	180	Ala to Val
637	A	G	193	Asp to Gly

5

Example 4. In-frame Cloning

NOV45b

10 For NOV45b, the cDNA coding for the DOMAIN of NOV45a (CG50718-02) from residues 511 to 705 was targeted for “in-frame” cloning by PCR. The PCR template was based on the previously identified plasmid, when available, or on human cDNA(s).

Table IFC1A. Oligonucleotide primers used to clone the target cDNA sequence:

Primers	Sequences
F3	5'-AGATCT CCCCATGCCCCGGCAGTGTCCGGGTCC-3' (SEQ ID NO: 548)
R3	5'-CTCGAG GCTGGGCTCGCCGATCAGATCCTGCATGAC-3' (SEQ ID NO:549)

15 For downstream cloning purposes, the forward primer includes an in-frame BglII restriction site and the reverse primer contains an in-frame Xho I restriction site.

An amplified product was detected by agarose gel electrophoresis. The fragment was gel-purified and ligated into the pCR2.1 vector (Invitrogen, Carlsbad, CA) following the manufacturer’s recommendation. Twelve clones per PCR reaction were picked and
20 sequenced. The inserts were sequenced using vector-specific M13 Forward and M13 Reverse primers and the following gene-specific primers:

Table IFC1B. Gene-specific Primers

NO	Primers	Sequences
NOV45a	SF1	CCTGGAGCCTGAGACAGCG (SEQ ID NO: 550)
	SF2	AGCATTCCCTATTACAACTCCAGAA (SEQ ID NO: 551)
	SR1	GGTGTCCACCAGCAGCCAG (SEQ ID NO: 552)
	SR2	ATCACAGTGACCACCTCACTGAA (SEQ ID NO: 553)

NOV7

For NOV7, the cDNA coding for a domain of CG57595-01 from residue 2191 to 2450 was targeted for “in-frame” cloning by PCR. The PCR template is based on human cDNA(s).

The following oligonucleotide primers were used to clone the target cDNA sequence:

5

Table IFC2A. Oligonucleotide primers used to clone the target cDNA sequence:

Primers	Sequences
F5	5'-GAATTC TGTGCAAACGGGCACACGACTGCAACG-3' (SEQ ID NO:554)
R4	5'-CTCGAG GCACTGCTGGCCGCCAGCGGACTCCCGTG-3' (SEQ ID NO: 555)

For downstream cloning purposes, the forward primer includes an in-frame EcoRI restriction site and the reverse primer contains an in-frame XhoI restriction site.

10

An amplified product was detected by agarose gel electrophoresis. The fragment was gel-purified and ligated into the pCR2.1 vector (Invitrogen, Carlsbad, CA) following the manufacturer’s recommendation. Twelve clones per PCR reaction were picked and sequenced. The inserts were sequenced using vector-specific M13 Forward and M13 Reverse primers and the following gene-specific primers:

15

Table IFC2B. Gene-specific Primers

NOV	Primers	Sequences
NOV7	SF1	TTGCTCTGCCGCAACCAC (SEQ ID NO: 556)
	SF2	AGCTATGGGGAGAAATGCGAG (SEQ ID NO: 557)
	SR1	CAGAGCAAGCAGTGGTCACG (SEQ ID NO: 558)
	SR2	TGTTATTCTGGCAGTTCACGC (SEQ ID NO: 559)

20

The cDNA coding for a domain of the full length form onf CG57595-01 between residues 1885 and 2450 was targeted for “in-frame” cloning by PCR. The PCR template is based on human cDNA(s).

The following oligonucleotide primers were used to clone the target cDNA sequence:

Table IFC2C. Oligonucleotide primers used to clone the target cDNA sequence:

Primers	Sequences
F4	5'-GAATTC CCCTGCCGCTGCTGTCCTCACC-3' (SEQ ID NO: 560)
R4	5'-CTCGAG GCACTGCTGGCCGCCAGCGGACTCCCGTG-3' (SEQ ID NO:561)

25

For downstream cloning purposes, the forward primer includes an in-frame EcoRI restriction site and the reverse primer contains an in-frame XhoI restriction site.

An amplified product was detected by agarose gel electrophoresis. The fragment was gel-purified and ligated into the pCR2.1 vector (Invitrogen, Carlsbad, CA) following the manufacturer's recommendation. Twelve clones per PCR reaction were picked and sequenced. The inserts were sequenced using vector-specific M13 Forward and M13 Reverse primers and the following gene-specific primers:

Table IFC2D. Gene-specific Primers

NOV	Primers	Sequences
NOV7	SF1	CTCTGAGAATGACTGTCGGATCA (SEQ ID NO: 562)
	SF2	TACCTCCTGCCTGGACTCTAAGG (SEQ ID NO: 563)
	SF3	CTCCTGGGCCTTCCTGTCCT (SEQ ID NO: 564)
	SF4	CTGCAACCGCCACAGTGAAT (SEQ ID NO: 565)
	SF5	CGTGTGCGTGAAGTCCAGAATA (SEQ ID NO: 566)
	SR1	AGAGGTGCAGGACCCATTGC (SEQ ID NO: 567)
	SR2	ACAGTTGGGTAGGAGGTGACAAG (SEQ ID NO: 568)
	SR3	CCCACATGTCAGCCCATCAC (SEQ ID NO: 569)
	SR4	ATTCAGTGTGGCGGTTGCAG (SEQ ID NO: 570)
	SR5	GGCCTCGTCTTCACTAGGACCC (SEQ ID NO:571)

NOV8

The cDNA coding for a domain of CG57452-01 from residue 156 to 815 was targeted for "in-frame" cloning by PCR. The PCR template is based on human cDNA(s).

The following oligonucleotide primers were used to clone the target cDNA sequence:

Table IFC3A. Oligonucleotide primers used to clone the target cDNA sequence:

Primers	Sequences
F2	5'-GGATCC TACTATGCCACAGTGAATGAGCTCACTCC-3' (SEQ ID NO:572)
R2	5'-CTCGAG CAAAACCTTGATGGCCAAGGTTAGAGTTGAATG-3' (SEQ ID NO: 573)

For downstream cloning purposes, the forward primer includes an in-frame BamHI restriction site and the reverse primer contains an in-frame XhoI restriction site.

An amplified product was detected by agarose gel electrophoresis. The fragment was gel-purified and ligated into the pCR2.1 vector (Invitrogen, Carlsbad, CA) following the manufacturer's recommendation. Twelve clones per PCR reaction were picked and sequenced. The inserts were sequenced using vector-specific M13 Forward and M13 Reverse primers and the following gene-specific primers:

NOV	Primers	Sequences
NOV8	SF1	GTTTCTTCCTTGTGTCCTTGTGCC (SEQ ID NO: 574)
	SF2	CCTTTGCCGGTCTACACATTGAAATACT (SEQ ID NO:575)
	SF3	TTGATGGTGTACAAGAAAGTGAGCCAG (SEQ ID NO: 576)
	SF4	CGAAGGAACTCCATCTGCACTGTGTAT (SEQ ID NO: 577)
	SF5	CAGTAAACATAATGGTGACAGATGTCAATG (SEQ ID NO:578)
	SR1	AAACATTGGACCCAAGTCATCTCC (SEQ ID NO: 579)
	SR2	GATGACCATTGTCTTGTTCAGCCTT (SEQ ID NO: 580)
	SR3	AATGCTGTTATCGAAAAGGTGTAAGTT (SEQ ID NO: 581)
	SR4	AATATACACAGTGCAGATGGAGTTCCT (SEQ ID NO:582)
	SR5	GTTTACTGTGGCAGTTGAGGTCCCAT (SEQ ID NO: 583)

The cDNA coding for a domain of the full length CG57452-01 from residue 728 to 1382 was targeted for “in-frame” cloning by PCR. The PCR template is based human cDNA(s).

The following oligonucleotide primers were used to clone the target cDNA sequence:

Table IFC3C. Oligonucleotide primers used to clone the target cDNA sequence:

Primers	Sequences
F3	5'-GGATCC AGAAATTTATCTGTGGTGGGAAGAAGAAGC-3' (SEQ ID NO: 584)
R1	5'-CTCGAG CCCTTCTGTGTATCCTAGACTTTCTCCTC-3' (SEQ ID NO:585)

For downstream cloning purposes, the forward primer includes an in-frame BamHI restriction site and the reverse primer contains an in-frame XhoI restriction site.

An amplified product was detected by agarose gel electrophoresis. The fragment was gel-purified and ligated into the pCR2.1 vector (Invitrogen, Carlsbad, CA) following the manufacturer’s recommendation. Twelve clones per PCR reaction were picked and sequenced. The inserts were sequenced using vector-specific M13 Forward and M13 Reverse primers and the following gene-specific primers:

Table IFC3d. Gene-specific Primers

NOV	Primers	Sequences
NOV8	SF1	ACTACCATCCTTCAAATAGAGGCCA (SEQ ID NO: 586)
	SF2	CACAACAGTTTATGCTGAAGATGCAGAC (SEQ ID NO:587)
	SF3	ATGGTTGGTGTAAATTTCTGCTGCTG (SEQ ID NO: 588)
	SF4	AGAGTGAAGGCTACTGATAAAGATACTGGC (SEQ ID NO:589)
	SF5	AAATCTTGGATCGCTATGTTTCAGGA (SEQ ID NO: 590)

SR1	TAGTCCCAGCTGGCAAATTCTCTTCAA (SEQ ID NO: 591)
SR2	ATAGGTGTACCCTTGACTGCATCCG (SEQ ID NO: 592)
SR3	CCTTTGGTGGCAAGTTCACTTACTG (SEQ ID NO: 593)
SR4	CAGAAGTAAACATTCTTGCATCTTCAG (SEQ ID NO: 594)
SR5	CATAGCGATCCAAGATTTCTGTAAGAT (SEQ ID NO: 595)

NOV11

The cDNA coding for a domain of CG57488-03 from residue 121 to 741 was targeted for “in-frame” cloning by PCR. The PCR template is based on human cDNA(s).

The following oligonucleotide primers were used to clone the target cDNA sequence:

Table IFC4A. Oligonucleotide primers used to clone the target cDNA sequence:

Primers	Sequences
F1	5'-AGATCT CAGCCTCAGGCCCCGGGTACTTGATTGCAGC-3'(SEQ ID NO: 596)
R1	5'-AAGCTT AGAAACATCATAATCTTCCAGTTCCTGG-3' (SEQ ID NO:597) .

For downstream cloning purposes, the forward primer includes an in-frame BglII restriction site and the reverse primer contains an in-frame HindIII restriction site.

Table IFC4B. Gene-specific Primers

NOV	Primers	Sequences
NOV11	SF1	GGACAAGCCTGTGTACAGACCCC (SEQ ID NO: 598)
	SF2	GGTATATCCAAGACCTGGACGCC (SEQ ID NO: 599)
	SF3	CAGCTGGTGGACATCCGGTACT (SEQ ID NO: 600)
	SF4	GTACTCCCCCAGCCAGTGCTACCT (SEQ ID NO: 601)
	SF5	CTCTCTTCATCTGGCCGTGACC (SEQ ID NO: 602)
	SR1	TCTGGATGAATACAGAAGCGCCC (SEQ ID NO: 603)
	SR2	GCGGGTCAATCAGAAGCTCAAAC (SEQ ID NO: 604)
	SR3	CTTGGAGTACCGGATGTCCACCAG (SEQ ID NO: 605)
	SR4	AGGGAGAGGTAGCTGGGCAGGTACTGA (SEQ ID NO: 606)
	SR5	CAGATGAAGAGAGGTCACACACACG (SEQ ID NO: 607)

The cDNA coding for a domain of the full-length protein CG57488-03 residue 119 to 741. was targeted for “in-frame” cloning by PCR. The PCR template is human cDNA(s).

The following oligonucleotide primers were used to clone the target cDNA sequence:

Table IFC4C. Oligonucleotide primers used to clone the target Cdna sequence:

Primers	Sequences
F1	5'-AGATCT CAGCCTCAGGCCCGGGTACTTGATTGCAGC-3'(SEQ ID NO: 608)

R1	5'-AAGCTT AGAAACATCATAATCTTCCAGTTCCTGG-3' (SEQ ID NO: 609)
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For downstream cloning purposes, the forward primer includes an in-frame BglII restriction site and the reverse primer contains an in-frame HindIII restriction site.

Table IFC4D. Gene-specific Primers

NOV	Primers	Sequences
NOV11	SF1	GGACAAGCCTGTGTACAGACCCC (SEQ ID NO: 610)
	SF2	GGTATATCCAAGACCTGGACGCC (SEQ ID NO: 611)
	SF3	CAGCTGGTGGACATCCGGTACT (SEQ ID NO: 612)
	SF4	GTACTCCCCCAGCCAGTGCTACCT (SEQ ID NO: 613)
	SF5	CTCTCTTCATCTGGCCGTGACC (SEQ ID NO: 614)
	SR1	TCTGGATGAATACAGAAGCGCCC (SEQ ID NO: 615)
	SR2	GCGGGTCAATCAGAAGCTCAAAC (SEQ ID NO: 616)
	SR3	CTTGGAGTACCGGATGTCCACCAG (SEQ ID NO: 617)
	SR4	AGGGAGAGGTAGCTGGGCAGGTACTGA (SEQ ID NO: 618)
	SR5	CAGATGAAGAGAGGTCACACACACG (SEQ ID NO: 619)

5

NOV52

For NOV52, the cDNA coding for the full-length NOV52 (CG57748-01) was targeted for “in-frame” cloning by PCR. The PCR template was based on the previously identified plasmid, when available, or on human cDNA(s).

10

Table IFC5A. Oligonucleotide primers used to clone the target cDNA sequence:

Primers	Sequences
F2	5'-AAGCTTATCTGGCAGTGTGGTGGGGTTCTGGAAAC -3' (SEQ ID NO: 620)
R1	5'-CTCGAGTAACATGCGCTCTTTGAAGAACCATTCTGATG-3' (SEQ ID NO: 621)

For downstream cloning purposes, the forward primer includes an in-frame HindIII restriction site and the reverse primer contains an in-frame Xho I restriction site.

15 An amplified product was detected by agarose gel electrophoresis. The fragment was gel-purified and ligated into the pCR2.1 vector (Invitrogen, Carlsbad, CA) following the manufacturer’s recommendation. Twelve clones per PCR reaction were picked and sequenced. The inserts were sequenced using vector-specific M13 Forward and M13 Reverse primers and the following gene-specific primers:

R3	5'- CTCGAGCAAACCTTAAGTCAACAATTATATGTTCAAA-3' (SEQ ID NO:633)
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For downstream cloning purposes, the forward primer includes an in-frame BamHI restriction site and the reverse primer contains an in-frame Xho I restriction site.

An amplified product was detected by agarose gel electrophoresis. The fragment was gel-purified and ligated into the pCR2.1 vector (Invitrogen, Carlsbad, CA) following the manufacturer's recommendation. Twelve clones per PCR reaction were picked and sequenced. The inserts were sequenced using vector-specific M13 Forward and M13 Reverse primers and the following gene-specific primers:

Table IFC6B. Gene-specific Primers

NOV	Primers	Sequences
NOV54	SF1	TGTTTCATTGAAGGGAACAAAATAGAAA (SEQ ID NO:634)
	SF2	AGGAAAAGAAGCTAAATGACGTGACCA (SEQ ID NO: 635)
	SF3	ATCAGGTCTTTGTGGTGGTAGCCC (SEQ ID NO: 636)
	SF4	ATGCGGAGTTTGTGATATCGATGGAA (SEQ ID NO: 637)
	SF5	ATGACCCTGCAGCCCTTTTCTTTTA (SEQ ID NO: 638)
	SR1	AGGTATTCAAGATGAAAAAGTCCAGCA (SEQ ID NO:639)
	SR2	TGATACTCTGGTGGACCAATACACAGC (SEQ ID NO: 640)
	SR3	CATCGATGAGAATGGCCTTACAGC (SEQ ID NO: 641)
	SR4	TGAACCACTCGTGCAGTGACTGGTAAG (SEQ ID NO: 642)
	SR5	GATGGAAGAGCTTGGATCTCCACAA (SEQ ID NO: 643)

NOV56

The cDNA coding for a domain of the full length CG57348-01 from residues 202 to 343 was targeted for "in-frame" cloning by PCR. The PCR template is based on human cDNA(s).

Table IFC7A. Oligonucleotide primers used to clone the target cDNA sequence:

Primers	Sequences
F2	5'-GGATCC TTGATTGAAAGTGGGAAGGAAGAAGGAATG-3' (SEQ ID NO: 644)
R1	5'-CTCGAG ATGCTTCAGCCACGGTGGGCTTCAATGGAAGC-3' (SEQ ID NO: 645)

For downstream cloning purposes, the forward primer includes an in-frame BamHI restriction site and the reverse primer contains an in-frame Xho I restriction site.

An amplified product was detected by agarose gel electrophoresis. The fragment was gel-purified and ligated into the pCR2.1 vector (Invitrogen, Carlsbad, CA) following the

manufacturer's recommendation. Twelve clones per PCR reaction were picked and sequenced. The inserts were sequenced using vector-specific M13 Forward and M13 Reverse primers and the following gene-specific primers:

Table IFC7B. Gene-specific Primers

NOV	Primers	Sequences
NOV56	SF1	CTCTGTATGCACAGGACCCTTCC (SEQ ID NO: 646)
	SF2	CAAACGACGACATCGACGG (SEQ ID NO: 647)
	SR1	CTCCCGTTTCTTGGCGTCG (SEQ ID NO: 648)
	SR2	GGTTTGGCAGTTCCACATT (SEQ ID NO: 649)

NOV60

The cDNA coding for a domain for the full length CG57574-01 from residue 18 to 275 was targeted for "in-frame" cloning by PCR. The PCR template is based on human cDNA(s).

Table IFC8A. Oligonucleotide primers used to clone the target cDNA sequence:

Primers	Sequences
F1	5'- GGATCC AAATCGTGTGCTCCAAATAAAGCAGATGTCATT-3' (SEQ ID NO: 650)
R1	5'- CTCGAG TCCCCCGGTCTGGTCTCGCAGGAGGCG-3' (SEQ ID NO: 651)

For downstream cloning purposes, the forward primer includes an in-frame BamHI restriction site and the reverse primer contains an in-frame Xho I restriction site.

An amplified product was detected by agarose gel electrophoresis. The fragment was gel-purified and ligated into the pCR2.1 vector (Invitrogen, Carlsbad, CA) following the manufacturer's recommendation. Twelve clones per PCR reaction were picked and sequenced. The inserts were sequenced using vector-specific M13 Forward and M13 Reverse primers and the following gene-specific primers:

Table IFC8B. Gene-specific Primers

NOV	Primers	Sequences
NOV60	SF1	AAAAACCAGCCTGTCAACTACTCCTTCTC (SEQ ID NO: 652)
	SF2	ACTTCATGTATCCCTTGCAGTGGC (SEQ ID NO: 653)
	SR1	GTGGTGTTCATTGGAAACGATGTG (SEQ ID NO: 654)
	SR2	ATACATGAAGTCAGCCGAGGGGGT (SEQ ID NO: 655)

Two parallel PCR reactions were set up using a total of 0.5-1.0 ng human pooled cDNAs as template for each reaction. The pool is composed of 5 micrograms of each of the following human tissue cDNAs: adrenal gland, whole brain, amygdala, cerebellum, thalamus, bone marrow, fetal brain, fetal kidney, fetal liver, fetal lung, heart, kidney, liver, lymphoma,

Burkitt's Raji cell line, mammary gland, pancreas, pituitary gland, placenta, prostate, salivary gland, skeletal muscle, small Intestine, spleen, stomach, thyroid, trachea, uterus.

When the tissue of expression is known and available, the second PCR was performed using the above primers and 0.5ng-1.0 ng of one of the following human tissue cDNAs:

5 skeleton muscle, testis, mammary gland, adrenal gland, ovary, colon, normal cerebellum, normal adipose, normal skin, bone marrow, brain amygdala, brain hippocampus, brain substantia nigra, brain thalamus, thyroid, fetal lung, fetal liver, fetal brain, kidney, heart, spleen, uterus, pituitary gland, lymph node, salivary gland, small intestine, prostate, placenta, spinal cord, peripheral blood, trachea, stomach, pancreas, hypothalamus.

10 The reaction mixtures contained 2 microliters of each of the primers (original concentration: 5 pmol/ul), 1 microliter of 10mM dNTP (Clontech Laboratories, Palo Alto CA) and 1 microliter of 50xAdvantage-HF 2 polymerase (Clontech Laboratories) in 50 microliter-reaction volume. The following reaction conditions were used:

PCR condition 1:

- 15 a) 96°C 3 minutes
b) 96°C 30 seconds denaturation
c) 60°C 30 seconds, primer annealing
d) 72°C 6 minutes extension

20 Repeat steps b-d 15 times

- e) 96°C 15 seconds denaturation
f) 60°C 30 seconds, primer annealing
g) 72°C 6 minutes extension

25 Repeat steps e-g 29 times

- e) 72°C 10 minutes final extension

PCR condition 2:

- 30 a) 96°C 3 minutes
b) 96°C 15 seconds denaturation
c) 76°C 30 seconds, primer annealing, reducing the temperature by 1 °C per cycle
d) 72°C 4 minutes extension

35 Repeat steps b-d 34 times

- e) 72°C 10 minutes final extension

OTHER EMBODIMENTS

Although particular embodiments have been disclosed herein in detail, this has been done by way of example for purposes of illustration only, and is not intended to be limiting with respect to the scope of the appended claims, which follow. In particular, it is

5 contemplated by the inventors that various substitutions, alterations, and modifications may be made to the invention without departing from the spirit and scope of the invention as defined by the claims. The choice of nucleic acid starting material, clone of interest, or library type is believed to be a matter of routine for a person of ordinary skill in the art with knowledge of the embodiments described herein. Other aspects, advantages, and modifications considered to be
10 within the scope of the following claims.